STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 180656

TO: Andrew D Kosar **Location: 3c04 / 3c18** **Tuesday, March 14, 2006** **Art Unit: 1654** **Phone: 571-272-0913** **Serial Number: 10 / 019786**	**From: Jan Delaval** **Location: Biotech-Chem Library** **Remsen 1a51** **Phone: 571-272-2504** **jan.delaval@uspto.gov**

Search Notes

Andrew -

The library never received rush authorization for your search request(s).

Jan

STIC-Biotech/ChemLib 180656

From: ANDREW KOSAR [andrew.kosar@uspto.gov]
Sent: Monday, February 27, 2006 12:30 PM
To: STIC-Biotech/ChemLib
Subject: Database Search Request, Serial Number: 10/109,786

10/019786

Requester:
ANDREW KOSAR (P/1654)
Art Unit:
GROUP ART UNIT 1654
Employee Number:
80341
Office Location:
REM 03C04
Phone Number:
(571)272-0913
Mailbox Number:
REM 3c04

Case serial number:
10/109,786 10/019786
Class 7 Subclass(es):

Earliest Priority Filing Date:

Format preferred for results:
Paper
Search Topic Information:
Please search:
A sustained release composition comprising:
1) a pharmacologically active substance or its salt,
2) a hydroxynaphthoic acid or its salt, and
3) a lactic acid-glycolic acid polymer or its salt

Special Instructions and Other Comments:
Rush search approved. Please forward as necessary to STIC.
Christopher Low
SPE 1614 / TCAR 1600
REM 3E88 / (571) 272-0951

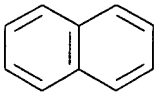
never received

****
Searcher: [illegible]
Searcher Phone:
Date Searcher Picked up: 3/14/06
Date completed: 3/14/06
Searcher Prep Time: 15
Online Time: 150

****
Type of Search
NA#_____ AA#:_____
S/L:_____ Oligomer:_____
Encode/Transl:_____
Structure #:_____Text:✓
Inventor:_____ Litigation:___

****
Vendors and cost where applicable
STN:✓
DIALOG:
QUESTEL/ORBIT:
LEXIS/NEXIS:
SEQUENCE SYSTEM:
WWW/Internet:
Other (Specify):

```
=> fil reg
FILE 'REGISTRY' ENTERED AT 07:18:19 ON 14 MAR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   12 MAR 2006  HIGHEST RN 876514-29-3
DICTIONARY FILE UPDATES:  12 MAR 2006  HIGHEST RN 876514-29-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> d l75 ide can tot

L75  ANSWER 1 OF 5  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   30440-92-7  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   Naphthalenecarboxylic acid, hydroxy- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Naphthoic acid, hydroxy- (7CI)
OTHER NAMES:
CN   Hydroxynaphthoic acid
MF   C11 H8 O3
CI   IDS, COM
LC   STN Files:   AGRICOLA, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMLIST, CIN,
       PIRA, PROMT, TOXCENTER, USPATFULL
     Other Sources:   EINECS**
         (**Enter CHEMLIST File for up-to-date regulatory information)
```



D1—OH

D1—CO_2H

71 REFERENCES IN FILE CA (1907 TO DATE)
14 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
71 REFERENCES IN FILE CAPLUS (1907 TO DATE)
6 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 143:163081

REFERENCE 2: 141:197401

REFERENCE 3: 140:363026

REFERENCE 4: 140:303407

REFERENCE 5: 137:294769

REFERENCE 6: 134:305328

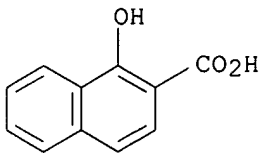
REFERENCE 7: 134:140601

REFERENCE 8: 134:120954

REFERENCE 9: 131:250398

REFERENCE 10: 131:106841

L75 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN **18396-51-5** REGISTRY
ED Entered STN: 16 Nov 1984
CN 2-Naphthalenecarboxylic acid, 1-hydroxy-, monosodium salt (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Naphthoic acid, 1-hydroxy-, monosodium salt (8CI)
OTHER NAMES:
CN 1-Hydroxy-2-naphthalenecarboxylic acid sodium salt
CN 1-Hydroxy-2-naphthoic acid sodium salt
CN Sodium 1-hydroxy-2-naphthoate
CN Sodium 1-hydroxynaphthalene-2-carboxylate
MF C11 H8 O3 . Na
LC STN Files: BEILSTEIN*, CA, CAPLUS, DETHERM*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
CRN (86-48-6)



● Na

23 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
23 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 142:183474

REFERENCE 2: 142:183473

REFERENCE 3: 139:110465

REFERENCE 4: 134:260381

REFERENCE 5: 132:93411

REFERENCE 6: 131:246806

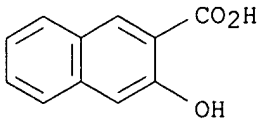
REFERENCE 7: 128:243950

REFERENCE 8: 126:277547

REFERENCE 9: 120:105457

REFERENCE 10: 119:225687

L75 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN **14206-62-3** REGISTRY
ED Entered STN: 16 Nov 1984
CN 2-Naphthalenecarboxylic acid, 3-hydroxy-, monosodium salt (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Naphthoic acid, 3-hydroxy-, monosodium salt (8CI)
OTHER NAMES:
CN 3-Hydroxy-2-naphthalenecarboxylic acid sodium salt
CN 3-Hydroxy-2-naphthoic acid sodium salt
CN Sodium 2-hydroxy-3-naphthoate
CN Sodium 3-hydroxy-2-naphthalenecarboxylate
CN Sodium 3-hydroxy-2-naphthoate
DR 94413-59-9
MF C11 H8 O3 . Na
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, DETHERM*, IFICDB, IFIPAT, IFIUDB, PS, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (92-70-6)



● Na

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

76 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
76 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 144:53397

REFERENCE 2: 144:8410

REFERENCE 3: 142:183474

REFERENCE 4: 142:183473

REFERENCE 5: 142:179460

REFERENCE 6: 140:359321

REFERENCE 7: 139:272638

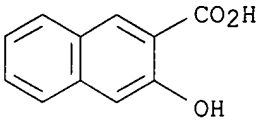
REFERENCE 8: 138:407241

REFERENCE 9: 138:339985

REFERENCE 10: 137:206536

L75 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN **92-70-6** REGISTRY
ED Entered STN: 16 Nov 1984
CN **2-Naphthalenecarboxylic acid, 3-hydroxy- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **2-Naphthoic acid, 3-hydroxy- (8CI)**
OTHER NAMES:
CN **β-Hydroxy-3-naphthoic acid**
CN **β-Hydroxynaphthoic acid**
CN **β-Oxynaphthoic acid**
CN **2-Hydroxy-3-carboxynaphthalene**
CN **2-Hydroxy-3-naphthalenecarboxylic acid**
CN **2-Hydroxy-3-naphthoic acid**
CN **2-Hydroxyl-3-naphthoic acid**
CN **2-Naphthol-3-carboxylic acid**
CN 3-Carboxy-2-naphthol
CN **3-Hydroxy-β-naphthoic acid**
CN **3-Hydroxy-2-naphthalenecarboxylic acid**
CN **3-Hydroxy-2-naphthoic acid**

CN **3-Naphthol-2-carboxylic acid**
CN BON
CN **BON acid**
CN BONA
CN C.I. Developer 20
CN Developer BON
CN Miketazol Developer ONS
CN Naphthol B.O.N.
CN NSC 3719
FS 3D CONCORD
DR 12235-60-8, 12235-61-9
MF **C11 H8 O3**
CI COM
LC STN Files: ANABSTR, BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MRCK*, MSDS-OHS, NIOSHTIC, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, ULIDAT, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1360 REFERENCES IN FILE CA (1907 TO DATE)
137 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1360 REFERENCES IN FILE CAPLUS (1907 TO DATE)
25 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 144:150646

REFERENCE 2: 144:141290

REFERENCE 3: 144:128693

REFERENCE 4: 144:117639

REFERENCE 5: 144:116710

REFERENCE 6: 144:95495

REFERENCE 7: 144:80168

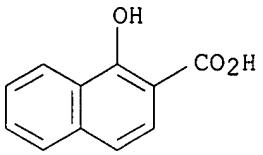
REFERENCE 8: 144:26542

REFERENCE 9: 144:24061

REFERENCE 10: 143:487405

L75 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN **86-48-6** REGISTRY
ED Entered STN: 16 Nov 1984
CN **2-Naphthalenecarboxylic acid, 1-hydroxy- (9CI)** (CA INDEX NAME)

OTHER CA INDEX NAMES:
CN **2-Naphthoic acid, 1-hydroxy- (8CI)**
OTHER NAMES:
CN **1-Hydroxy-2-naphthalenecarboxylic acid**
CN **1-Hydroxy-2-naphthoic acid**
CN **1-Naphthol-2-carboxylic acid**
CN 2-Carboxy-1-naphthol
CN NSC 3717
FS 3D CONCORD
MF **C11 H8 O3**
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, PIRA, SPECINFO, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

640 REFERENCES IN FILE CA (1907 TO DATE)
49 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
640 REFERENCES IN FILE CAPLUS (1907 TO DATE)
14 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 144:116710

REFERENCE 2: 144:24061

REFERENCE 3: 144:22659

REFERENCE 4: 143:460276

REFERENCE 5: 143:460093

REFERENCE 6: 143:402347

REFERENCE 7: 143:373312

REFERENCE 8: 143:260403

REFERENCE 9: 143:236287

REFERENCE 10: 143:229808

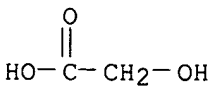
=> d l76 ide can tot

L76 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN

RN **34346-01-5** REGISTRY
ED Entered STN: 16 Nov 1984
CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Acetic acid, hydroxy-, polymer with 2-hydroxypropanoic acid (9CI)
OTHER NAMES:
CN (±)-2-Hydroxypropanoic acid-hydroxyacetic acid copolymer
CN Alzamer Depot
CN DL-Lactic acid-glycolic acid copolymer
CN dl-Lactic acid-glycolic acid copolymer
CN dl-Lactic acid-glycolic acid polymer
CN GC-Membrane
CN Glycolic acid-DL-lactic acid copolymer
CN Glycolic acid-dl-lactic acid copolymer
CN Glycolic acid-lactic acid copolymer
CN Glycolic acid-lactic acid polymer
CN Hydroxyacetic acid-(±)-2-hydroxypropanoic acid copolymer
CN Hydroxyacetic acid-2-hydroxypropionic acid copolymer
CN Hydroxyacetic acid-lactic acid copolymer
CN Lactic acid-glycolic acid copolymer
CN Lactic acid-glycolic acid polymer
CN PLGA 5010
CN PLGA 5020
CN PLGA 75-65
CN PLGA 7510
CN PLGA 7520
CN Poly(DL-lactic acid-glycolic acid)
CN Poly(glycolic acid-co-DL-lactic acid)
CN Poly(glycolic acid-lactic acid)
CN Poly(lactic acid-glycolic acid)
CN Resolut
CN Resolut LT
CN Resolut ST
CN Resomer RG 858
DR 59199-59-6, 66327-52-4, 153439-97-5, 265647-91-4
MF **(C3 H6 O3 . C2 H4 O3)x**
CI PMS, COM
PCT Polyester, Polyester formed
LC STN Files: AGRICOLA, BIOSIS, BIOTECHNO, CA, CAPLUS, CIN, CSCHEM, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, PATDPASPC, TOXCENTER, TULSA, USPAT2, USPATFULL

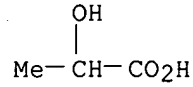
CM 1

CRN 79-14-1
CMF C2 H4 O3



CM 2

CRN 50-21-5
CMF C3 H6 O3



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2234 REFERENCES IN FILE CA (1907 TO DATE)
46 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2240 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 144:219215

REFERENCE 2: 144:219195

REFERENCE 3: 144:219117

REFERENCE 4: 144:219116

REFERENCE 5: 144:219101

REFERENCE 6: 144:218946

REFERENCE 7: 144:205768

REFERENCE 8: 144:199034

REFERENCE 9: 144:199013

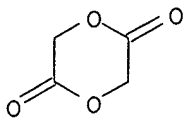
REFERENCE 10: 144:198677

L76 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN
RN **26780-50-7** REGISTRY
ED Entered STN: 16 Nov 1984
CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,4-Dioxane-2,5-dione, polymer with 3,6-dimethyl-1,4-dioxane-2,5-dione (9CI)
CN p-Dioxane-2,5-dione, 3,6-dimethyl-, polyester with p-dioxane-2,5-dione (8CI)
CN p-Dioxane-2,5-dione, polyester with 3,6-dimethyl-p-dioxane-2,5-dione (8CI)
OTHER NAMES:
CN 1,4-Dioxane-2,5-dione-1-DL-3,6-dimethyl-1,4-dioxane-2,5-dione copolymer
CN 3,6-Dimethyl-1,4-dioxane-2,5-dione-1,4-dioxane-2,5-dione copolymer
CN Atrigel
CN Diglycolide-DL-dilactide copolymer
CN DL-Lactide-glycolide copolymer
CN Ethicon W 9045
CN Glycolide-dl-lactide copolymer
CN Glycolide-DL-lactide copolymer
CN Glycolide-DL-lactide polymer
CN Glycolide-lactide copolymer
CN Glycolide-lactide polymer
CN Lactel BP 0100
CN Lactide-diglycolide copolymer
CN Lactide-glycolide copolymer
CN Medisorb

CN Medisorb (polymer)
CN Medisorb 5050DL
CN Medisorb 5050DL High IV
CN Medisorb 5050DL-PLG2A
CN Medisorb 5050DL-PLG4A
CN Medisorb 5050DL-PLG5A
CN Medisorb 5050DL2A
CN Medisorb 7525DL
CN Medisorb 7525DL High IV
CN Medisorb 8515DL
CN Medisorb 8515DL-PLG6A
CN Medisorb 8515DLC01
CN PLG
CN Poly(dl-lactide-co-glycolide)
CN Poly(DL-lactide-glycolide)
CN Poly(glycolide-co-lactide)
CN Poly(glycolide-lactide)
CN Poly(lactide-co-glycolide)
CN Poly-(DL)-lactide-co-glycolide
CN Polyglactin
CN Polyglactin 370
CN Polyglactin 910
CN Purac PDLG
CN Purasorb PDLG
CN Purasorb PLGA
CN Resomer 502H
CN Resomer 503
CN Resomer R 6-503
CN Resomer RG 206
CN Resomer RG 501H
CN Resomer RG 502
CN Resomer RG 502H
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
DR 130953-65-0, 119652-89-0, 31213-75-9, 107760-14-5, 339986-68-4, 444725-05-7, 460731-87-7
MF **(C6 H8 O4 . C4 H4 O4)x**
CI PMS, COM
PCT Polyester, Polyester formed
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, NIOSHTIC, PIRA, PROMT, TOXCENTER, USAN, USPAT2, USPATFULL

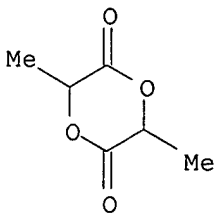
CM 1

CRN 502-97-6
CMF C4 H4 O4



CM 2

CRN 95-96-5
CMF C6 H8 O4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3547 REFERENCES IN FILE CA (1907 TO DATE)
65 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3570 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 144:219378

REFERENCE 2: 144:219353

REFERENCE 3: 144:219092

REFERENCE 4: 144:219040

REFERENCE 5: 144:218975

REFERENCE 6: 144:218971

REFERENCE 7: 144:218967

REFERENCE 8: 144:218966

REFERENCE 9: 144:218957

REFERENCE 10: 144:218950

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 07:18:39 ON 14 MAR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 14 Mar 2006 VOL 144 ISS 12
FILE LAST UPDATED: 13 Mar 2006 (20060313/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot l73

L73 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:99313 HCAPLUS
DN 142:183474
ED Entered STN: 04 Feb 2005
TI Controlled release pharmaceutical compositions containing polymers
IN Cook, Gary P.
PA PR Pharmaceuticals, USA
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 63-6 (**Pharmaceuticals**)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005009357	A2	20050203	WO 2004-US22817	20040715
WO 2005009357	A3	20051124		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, US
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-489402P P 20030723

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2005009357	ICM	A61K
	IPCI	A61K [ICM,7]; A61K0009-14 [ICS,7]; A61K0009-16 [ICS,7]
	IPCR	A61K [I,S]

AB The compns. disclosed herein are for use as controlled release therapeutics for the treatment of a wide variety of diseases. In particular, the compns. provide water-soluble bioactive agents, organic ions and polymers where the bioactive agent is efficiently released over time with minimal degradation products. The resulting controlled release composition is capable of administration in a decreased dose volume due to the high drug content and predominance of non-degraded bioactive agent after release. Addnl., the compns., of the present invention are capable of long term sustained release. Thus, octreotide acetate was encapsulated in PLGA polymer to give the microparticles.

ST controlled release pharmaceutical polymer
IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(caprolactone-based; controlled release pharmaceutical compns. containing polymers)
IT Antihistamines

Antitumor agents
Antiulcer agents
Asthma
Bronchodilators
Cardiovascular agents
Cardiovascular system, disease
Dissolution
Drug bioavailability
Neoplasm
Nervous system, disease
Nervous system agents
Opioid antagonists
Particle size distribution
Ulcer
Vasodilators
(controlled release pharmaceutical compns. containing polymers)

IT Antigens
Carbohydrates, biological studies
Hormones, animal, biological studies
Nucleic acids
Peptides, biological studies
Polyanhydrides
Polycarbonates, biological studies
Polyesters, biological studies
Polymer blends
Polymers, biological studies
Polyoxyalkylenes, biological studies
Polyoxymethylenes, biological studies
Polyurethanes, biological studies
Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release pharmaceutical compns. containing polymers)

IT Drug delivery systems
(controlled-release; controlled release pharmaceutical compns. containing polymers)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dilactone-based; controlled release pharmaceutical compns. containing polymers)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glycolide-based; controlled release pharmaceutical compns. containing polymers)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxycarboxylic acid-based; controlled release pharmaceutical compns. containing polymers)

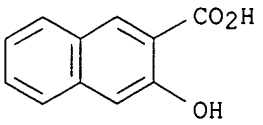
IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lactic acid-based; controlled release pharmaceutical compns. containing polymers)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lactide; controlled release pharmaceutical compns. containing polymers)

IT Encapsulation
(microencapsulation; controlled release pharmaceutical compns. containing polymers)

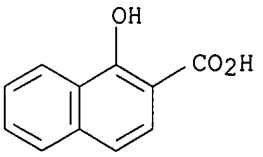
IT Drug delivery systems
(microparticles; controlled release pharmaceutical compns. containing polymers)

IT Polyethers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ortho ester group-containing; controlled release pharmaceutical compns. containing polymers)
IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyamide-; controlled release pharmaceutical compns. containing polymers)
IT Polyamides, biological studies
Polyethers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyester-; controlled release pharmaceutical compns. containing polymers)
IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyether-; controlled release pharmaceutical compns. containing polymers)
IT 9034-40-6, LHRH
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(agonists; controlled release pharmaceutical compns. containing polymers)
IT 79517-01-4, Octreotide acetate
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release pharmaceutical compns. containing polymers)
IT 6640-22-8, Sodium pamoate
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(controlled release pharmaceutical compns. containing polymers)
IT 135467-16-2P 834894-41-6P 834894-42-7P 834894-79-0P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(controlled release pharmaceutical compns. containing polymers)
IT 50-56-6, Oxytocin, biological studies 54-21-7, Sodium salicylate 361-09-1, Sodium cholate 532-02-5, Sodium 2-naphthalenesulfonate 532-32-1 6233-83-6, Oxytocin acetate 9004-10-8, Insulin, biological studies 14047-56-4 **14206-62-3**, Sodium 3-**hydroxy**-2-**naphthoate** 17273-79-9, Sodium 2-naphthoate **18396-51-5**, Sodium 1-**hydroxy**-2-**naphthoate** 23520-54-9, Sodium salicylsalicylate 24980-41-4, Polycaprolactone 25248-42-4, Polycaprolactone 25322-68-3D, Polyethylene glycol, copolymers 25832-58-0, Trifluoromethyl p-toluic acid sodium salt 26009-03-0, Polyglycolide 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Poly(lactic acid) 26124-68-5, Poly(glycolic acid) 26202-08-4, Polyglycolide 26680-10-4, Polylactide **26780-50-7**, **Glycolide-lactide** copolymer 29223-92-5 31621-87-1, Polydioxanone **34346-01-5**, **Glycolic** acid-**lactic** acid copolymer 51110-01-1, Somatostatin 53714-56-0, Leuprolide 74381-53-6, Leuprolide acetate 834894-43-8, Sodium 2,3-naphthalenedicarboxylate
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(controlled release pharmaceutical compns. containing polymers)
IT **14206-62-3**, Sodium 3-**hydroxy**-2-**naphthoate**
18396-51-5, Sodium 1-**hydroxy**-2-**naphthoate**
26780-50-7, **Glycolide-lactide** copolymer
34346-01-5, **Glycolic** acid-**lactic** acid copolymer
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(controlled release pharmaceutical compns. containing polymers)
RN 14206-62-3 HCAPLUS
CN 2-Naphthalenecarboxylic acid, 3-hydroxy-, monosodium salt (9CI) (CA INDEX NAME)



● Na

RN 18396-51-5 HCAPLUS
CN 2-Naphthalenecarboxylic acid, 1-hydroxy-, monosodium salt (9CI) (CA INDEX NAME)

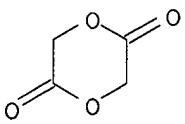


● Na

RN 26780-50-7 HCAPLUS
CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione (9CI) (CA INDEX NAME)

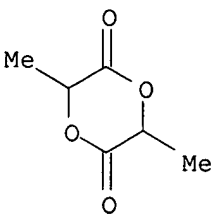
CM 1

CRN 502-97-6
CMF C4 H4 O4



CM 2

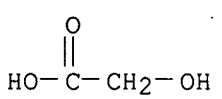
CRN 95-96-5
CMF C6 H8 O4



RN 34346-01-5 HCAPLUS
CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA INDEX NAME)

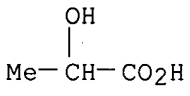
CM 1

CRN 79-14-1
CMF C2 H4 O3



CM 2

CRN 50-21-5
CMF C3 H6 O3



L73 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:99312 HCAPLUS
DN 142:183473
ED Entered STN: 04 Feb 2005
TI Preparation of controlled release pharmaceutical formulations containing polymers
IN Gary, P. Cook
PA PR Pharmaceuticals, USA
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 63-6 (**Pharmaceuticals**)
Section cross-reference(s): **1**
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005009356	A2	20050203	WO 2004-US22816	20040715
	WO 2005009356	A3	20050609		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-487663P P 20030715

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2005009356	ICM	A61K
	IPCI	A61K [ICM,7]
	IPCR	A61F0002-02 [I,A]; A61F0002-02 [I,C]; A61K [I,S]; A61K0009-50 [I,A]; A61K0009-50 [I,C]; A61K0047-30 [I,A]; A61K0047-30 [I,C]

AB The methods disclosed herein are of use for the production of controlled release compns. In particular, the methods provide the contacting of an organic phase containing a bioactive agent and a polymer with an aqueous phase containing an organic ion to create controlled release compns. containing bioactive agents. The present invention also includes controlled release compns. including a polymer, an organic ion and a bioactive agent. The present invention also includes methods of using such controlled release compns. The usefulness of the present invention is that the methods result in the production of controlled release compns. containing bioactive agent capable of administration in a concentrated low-dose form, having low burst and reduced production of degraded bioactive agent. Thus, octreotide acetate was encapsulated in PLGA polymer to give the microparticles.

ST controlled release pharmaceutical polymer

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(caprolactone-based; preparation of controlled release pharmaceutical formulations containing polymers)

IT Drug delivery systems
(controlled-release; preparation of controlled release pharmaceutical formulations containing polymers)

IT Solvents
(cosolvents; preparation of controlled release pharmaceutical formulations containing polymers)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dilactone-based; preparation of controlled release pharmaceutical formulations containing polymers)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glycolide-based; preparation of controlled release pharmaceutical formulations containing polymers)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxycarboxylic acid-based; preparation of controlled release pharmaceutical formulations containing polymers)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lactic acid-based; preparation of controlled release pharmaceutical formulations containing polymers)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lactide; preparation of controlled release pharmaceutical formulations containing polymers)

IT Encapsulation
(microencapsulation; preparation of controlled release pharmaceutical formulations containing polymers)

IT Drug delivery systems
(microparticles; preparation of controlled release pharmaceutical formulations containing polymers)

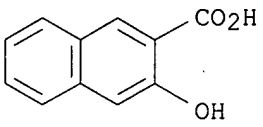
IT Drug delivery systems
(nanoparticles; preparation of controlled release pharmaceutical formulations containing polymers)
IT Polyethers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ortho ester group-containing; preparation of controlled release pharmaceutical
formulations containing polymers)
IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyamide-; preparation of controlled release pharmaceutical formulations containing polymers)
IT Polyamides, biological studies
Polyethers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyester-; preparation of controlled release pharmaceutical formulations containing polymers)
IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyether-; preparation of controlled release pharmaceutical formulations containing polymers)
IT Antihistamines
Antitumor agents
Antiulcer agents
Asthma
Bronchodilators
Cardiovascular agents
Cardiovascular system, disease
Dissolution
Drug bioavailability
Emulsifying agents
Neoplasm
Nervous system, disease
Nervous system agents
Opioid antagonists
Particle size distribution
Ulcer
Vasodilators
(preparation of controlled release pharmaceutical formulations containing polymers)
IT Polyoxyalkylenes, uses
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of controlled release pharmaceutical formulations containing polymers)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of controlled release pharmaceutical formulations containing polymers)
IT Carbohydrates, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of controlled release pharmaceutical formulations containing polymers)
IT Hormones, animal, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of controlled release pharmaceutical formulations containing polymers)
IT Nucleic acids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of controlled release pharmaceutical formulations containing polymers)

IT Peptides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of controlled release pharmaceutical formulations containing polymers)
IT Polyanhydrides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of controlled release pharmaceutical formulations containing polymers)
IT Polycarbonates, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of controlled release pharmaceutical formulations containing polymers)
IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of controlled release pharmaceutical formulations containing polymers)
IT Polymer blends
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of controlled release pharmaceutical formulations containing polymers)
IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of controlled release pharmaceutical formulations containing polymers)
IT Polyoxymethylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of controlled release pharmaceutical formulations containing polymers)
IT Polyurethanes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of controlled release pharmaceutical formulations containing polymers)
IT Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of controlled release pharmaceutical formulations containing polymers)
IT 64-17-5, EtOH, uses 64-19-7, Acetic acid, uses 67-56-1, MeOH, uses 67-63-0, Isopropanol, uses 67-64-1, Acetone, uses 67-68-5, DMSO, uses 68-12-2, DMF, uses 75-09-2, Methylene chloride, uses 100-51-6, Benzyl alcohol, uses 108-32-7, Propylene carbonate 141-78-6, EtOAc, uses 872-50-4, uses 25322-68-3, Polyethylene glycol
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of controlled release pharmaceutical formulations containing polymers)
IT 135467-16-2P 834894-41-6P 834894-42-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of controlled release pharmaceutical formulations containing polymers)
IT 50-56-6, Oxytocin, biological studies 54-21-7, Sodium salicylate 65-85-0, Benzoic acid, biological studies 361-09-1, Sodium cholate 532-02-5, Sodium 2-naphthalenesulfonate 532-32-1, Sodium benzoate 6640-22-8, Disodium pamoate 9002-89-5, Poly(vinyl alcohol) 9002-96-4, Vitamin E TPGS 9004-10-8, Insulin, biological studies 14047-56-4, Sodium succinate **14206-62-3**, Sodium 3-**hydroxy**-2-**naphthoate** 17273-79-9, Sodium 2-naphthoate **18396-51-5**, Sodium 1-**hydroxy**-2-**naphthoate** 23520-54-9, Sodium salicylsalicylate 24980-41-4, Polycaprolactone 25248-42-4, Polycaprolactone 25322-68-3D, Polyethylene glycol, copolymers 25832-58-0, Trifluoromethyl p-toluic acid sodium salt 26009-03-0,

Polyglycolide 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Poly(lactic acid) 26124-68-5, Polyglycolic acid 26202-08-4, Polyglycolide 26680-10-4, Poly(lactide) **26780-50-7**, **Glycolide-lactide** copolymer 29223-92-5 31621-87-1, PolyDioxanone **34346-01-5**, **Glycolic** acid-**lactic** acid copolymer 51110-01-1, Somatostatin 53714-56-0, Leuprolide 79517-01-4, Octreotide acetate 83150-76-9, Octreotide 834894-43-8, Sodium 2,3-naphthalenedicarboxylate
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(preparation of controlled release pharmaceutical formulations containing polymers)

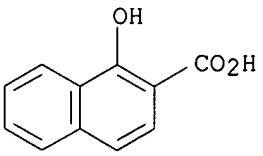
IT **14206-62-3**, Sodium 3-**hydroxy**-2-**naphthoate**
18396-51-5, Sodium 1-**hydroxy**-2-**naphthoate**
26780-50-7, **Glycolide-lactide** copolymer
34346-01-5, **Glycolic** acid-**lactic** acid copolymer
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(preparation of controlled release pharmaceutical formulations containing polymers)

RN 14206-62-3 HCAPLUS
CN 2-Naphthalenecarboxylic acid, 3-hydroxy-, monosodium salt (9CI) (CA INDEX NAME)



● Na

RN 18396-51-5 HCAPLUS
CN 2-Naphthalenecarboxylic acid, 1-hydroxy-, monosodium salt (9CI) (CA INDEX NAME)



● Na

RN 26780-50-7 HCAPLUS
CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione (9CI) (CA INDEX NAME)

CM 1

CRN 502-97-6
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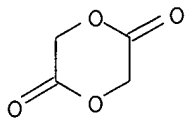
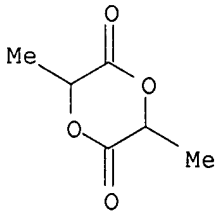


CM 2

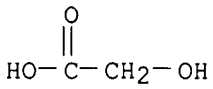
CRN 95-96-5
CMF C6 H8 O4



RN 34346-01-5 HCAPLUS
CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA INDEX NAME)

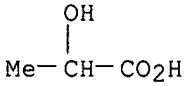
CM 1

CRN 79-14-1
CMF C2 H4 O3



CM 2

CRN 50-21-5
CMF C3 H6 O3



L73 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:465844 HCAPLUS
DN 137:37675
ED Entered STN: 21 Jun 2002
TI Medicinal compositions of nonpeptidyl gonadotropin-releasing hormone agonist or antagonist, process for producing the same and use thereof
IN Suzuki, Hiroshi; **Hata, Yoshio**

PA **Takeda Chemical Industries, Ltd., Japan**
SO PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM A61K0045-00
ICS A61K0031-519; A61K0031-4365; A61K0009-50; A61K0009-52; A61K0047-12; A61K0047-34; A61P0034-00; A61P0005-24; A61P0035-04; A61P0013-08; A61P0015-00; A61P0017-00; A61P0017-14; A61P0025-28; A61P0015-08; A61P0001-00; A61P0015-18; C07D0495-04
CC 63-6 (**Pharmaceuticals**)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002047722	A1	20020620	WO 2001-JP10956	20011214
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002021139	A5	20020624	AU 2002-21139	20011214
JP 2002326960	A2	20021115	JP 2001-380955	20011214
PRAI JP 2000-382431	A	20001215		
WO 2001-JP10956	W	20011214		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002047722	ICM	A61K0045-00
	ICS	A61K0031-519; A61K0031-4365; A61K0009-50; A61K0009-52; A61K0047-12; A61K0047-34; A61P0034-00; A61P0005-24; A61P0035-04; A61P0013-08; A61P0015-00; A61P0017-00; A61P0017-14; A61P0025-28; A61P0015-08; A61P0001-00; A61P0015-18; C07D0495-04
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	IPCR	A61K0031-00 [I,A]; A61K0031-00 [I,C]; A61K0031-4353 [I,C]; A61K0031-4365 [I,A]; A61K0031-519 [I,A]; A61K0031-519 [I,C]; A61K0047-12 [I,A]; A61K0047-12 [I,C]; A61K0047-34 [I,A]; A61K0047-34 [I,C]; C07D0333-00 [I,C]; C07D0333-38 [I,A]; C07D0471-00 [I,C]; C07D0471-04 [I,A]; C07D0487-00 [I,C]; C07D0487-04 [I,A]; C07D0495-00 [I,C]; C07D0495-04 [I,A]
	ECLA	A61K031/00+A; A61K031/4365; A61K031/519; C07D333/38; C07D471/04+221C+209C; C07D471/04+221B+209B; C07D471/04+235C+221C; C07D487/04+239C+209C; C07D487/04+239C+235C; C07D495/04+333B+239B
AU 2002021139	IPCI	A61K0045-00 [ICM,7]; A61K0031-519 [ICS,7]; A61K0031-4365 [ICS,7]; A61K0009-50 [ICS,7]; A61K0009-52 [ICS,7]; A61K0047-12 [ICS,7]; A61K0047-34 [ICS,7]; A61P0005-24 [ICS,7]; A61P0035-04 [ICS,7]; A61P0013-08

[ICS,7]; A61P0015-00 [ICS,7]; A61P0017-00 [ICS,7]; A61P0017-14 [ICS,7]; A61P0025-28 [ICS,7]; A61P0015-08 [ICS,7]; A61P0001-00 [ICS,7]; A61P0015-18 [ICS,7]; C07D0495-04 [ICS,7]

JP 2002326960 IPCI A61K0047-34 [ICM,7]; A61K0009-16 [ICS,7]; A61K0031-4365 [ICS,7]; A61K0031-522 [ICS,7]; A61K0045-00 [ICS,7]; A61K0047-12 [ICS,7]; A61P0001-00 [ICS,7]; A61P0005-24 [ICS,7]; A61P0013-08 [ICS,7]; A61P0015-00 [ICS,7]; A61P0015-08 [ICS,7]; A61P0015-18 [ICS,7]; A61P0017-10 [ICS,7]; A61P0017-14 [ICS,7]; A61P0025-28 [ICS,7]; A61P0035-00 [ICS,7]

OS MARPAT 137:37675

AB Disclosed are medicinal compns. comprising (i) a nonpeptidyl gonadotropin-releasing hormone agonist or antagonist, (ii) an organic acid or its salt, and (iii) a biodegradable polymer or its salt. These compns. can be efficiently produced, suffer from no trouble in quality control and can achieve a stable releasing speed over a long period of time, even in case where the nonpeptidyl GnRH agonist or antagonist is contained in a large amount regardless of the solubility, m.p. or crystallinity thereof. A compound 5-(N-benzyl-N-methylaminomethyl)-1-(2,6-difluorobenzyl)-6-[4-(3-methoxy ureide)phenyl]-3-phenylthieno[2,3-d]pyrimidine-2,4-(1H,3H)-dione was prepared and dissolved in dichloromethane with 3-**hydroxy**-2-**naphthoic acid** and polylactic acid. The solution was poured in polyvinyl alc. solution, emulsified, and freeze-dried with mannitol to obtain a microsphere. The microsphere showed controlled-release of the compound when s.c. administered in rats.

ST gonadotropin releasing hormone agonist antagonist controlled release microsphere

IT Ovulation
(accelerators; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Carboxylic acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aromatic, hydroxy; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Prostate gland, disease
(benign hyperplasia, treatment of; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Hyperplasia
(benign prostatic, treatment of; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biodegradable; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Sex hormones
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(disease related, treatment of; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Uterus, disease
(endometriosis, treatment of; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Hair preparations
(growth stimulants; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Uterus, disease
(hysteromyoma, treatment of; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Drug delivery systems

(injections, sustained release, microsphere; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Intestine, disease
(irritable bowel syndrome, treatment of; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lactic acid-based; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Uterus, neoplasm
(leiomyoma, treatment of; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Anti-Alzheimer's agents
Contraceptives
(medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Drug delivery systems
(microspheres, controlled-release; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Drug delivery systems
(microspheres, sustained-release, injections; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Ovary, disease
(multilocular ovarian syndrome, treatment of; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Puberty
(precocious puberty, treatment of; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Ovarian cycle
(premenstrual syndrome, treatment of; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Reproduction, animal
(regulation of; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Antitumor agents
(sex hormone-related tumor inhibitor; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT Acne
Alopecia
Alzheimer's disease
Amenorrhea
Dysmenorrhea
Sterility
(treatment of; medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT 9034-40-6, Gonadotropin-releasing hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT 308831-61-0P 392231-14-0P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT 69-72-7, Salicylic acid, biological studies **86-48-6**, 1-**Hydroxy**-2-**naphthoic acid** **92-70-6**, 3-**Hydroxy**-2-**naphthoic acid** 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Polylactic acid **34346-01-5**, **Lactic** acid-**glycolic** acid copolymer 174072-31-2 436805-94-6
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

IT 103-67-3, Benzylmethylamine 103-71-9, Phenylisocyanate, reactions 105-56-6, Ethyl cyano acetate 128-08-5, N-Bromosuccinimide 697-73-4, 2,6-Difluorobenzylchloride 5332-96-7, 4-Nitrophenylacetone 174072-80-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of nonpeptidic GnRH agonists or antagonists for microsphere composition containing organic acids and biodegradable polymers)

IT 174069-44-4P 174071-70-6P 174072-63-0P 174072-89-0P 174072-92-5P 174073-19-9P 174073-49-5P 392231-15-1P 392231-16-2P 392231-17-3P 392231-18-4P 392231-97-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of nonpeptidic GnRH agonists or antagonists for microsphere composition containing organic acids and biodegradable polymers)

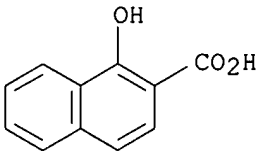
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

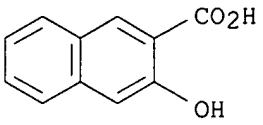
(1) Asta Medica Ag; JP 09509145 A 1995
(2) Asta Medica Ag; DE 4342092 A 1995 HCAPLUS
(3) Asta Medica Ag; US 5773032 A 1995 HCAPLUS
(4) Asta Medica Ag; EP 732934 A1 1995 HCAPLUS
(5) Asta Medica Ag; WO 9515767 A1 1995 HCAPLUS
(6) Sandoz Ltd; JP 06340543 A 1994 HCAPLUS
(7) Sandoz Ltd; EP 626170 A2 1994 HCAPLUS
(8) Takeda Chemical Industries Ltd; JP 08295693 A 1995 HCAPLUS
(9) Takeda Chemical Industries Ltd; US 5817819 A 1995 HCAPLUS
(10) Takeda Chemical Industries Ltd; EP 756599 A1 1995 HCAPLUS
(11) Takeda Chemical Industries Ltd; WO 9528405 A1 1995 HCAPLUS
(12) Takeda Chemical Industries Ltd; JP 09169768 A 1996 HCAPLUS
(13) Takeda Chemical Industries Ltd; US 6187788 A 1996 HCAPLUS
(14) Takeda Chemical Industries Ltd; EP 808317 A1 1996 HCAPLUS
(15) Takeda Chemical Industries Ltd; WO 9624597 A1 1996 HCAPLUS
(16) Takeda Chemical Industries Ltd; JP 10273447 A 1998 HCAPLUS
(17) Takeda Chemical Industries Ltd; WO 9832423 A1 1998 HCAPLUS
(18) Takeda Chemical Industries Ltd; EP 1048301 A1 1999 HCAPLUS
(19) Takeda Chemical Industries Ltd; JP 11269094 A 1999 HCAPLUS
(20) Takeda Chemical Industries Ltd; AU 9918897 A 1999 HCAPLUS
(21) Takeda Chemical Industries Ltd; WO 9936099 A1 1999 HCAPLUS
(22) Takeda Chemical Industries Ltd; WO 0056739 A1 2000 HCAPLUS
(23) Takeda Chemical Industries Ltd; EP 1163244 A1 2000 HCAPLUS
(24) Takeda Chemical Industries Ltd; JP 2001278884 A 2000 HCAPLUS
(25) Takeda Chemical Industries Ltd; US 6297379 A 2000 HCAPLUS
(26) Takeda Chemical Industries Ltd; JP 200181043 A 2001

IT **86-48-6**, 1-**Hydroxy**-2-**naphthoic acid**
92-70-6, 3-**Hydroxy**-2-**naphthoic acid**
34346-01-5, **Lactic** acid-**glycolic** acid copolymer
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(medicinal compns. containing nonpeptidic GnRH agonists or antagonists, organic acids, and biodegradable polymers)

RN 86-48-6 HCAPLUS
CN 2-Naphthalenecarboxylic acid, 1-hydroxy- (9CI) (CA INDEX NAME)



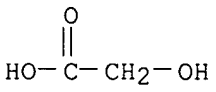
RN 92-70-6 HCAPLUS
CN 2-Naphthalenecarboxylic acid, 3-hydroxy- (9CI) (CA INDEX NAME)



RN 34346-01-5 HCAPLUS
CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA INDEX NAME)

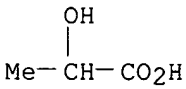
CM 1

CRN 79-14-1
CMF C2 H4 O3



CM 2

CRN 50-21-5
CMF C3 H6 O3



L73 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:63807 HCAPLUS
DN 134:120954
ED Entered STN: 26 Jan 2001
TI Sustained-release compositions, process for producing the same and use thereof
IN **Igari, Yasutaka; Hata, Yoshio; Yamamoto, Kazumichi**
PA **Takeda Chemical Industries, Ltd., Japan**
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA Japanese

IC ICM A61K0009-52
ICS A61K0038-09; A61K0047-12; A61K0047-34; A61P0035-00; A61P0005-24; A61P0013-08; A61P0015-00
CC 63-6 (**Pharmaceuticals**)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001005380	A1	20010125	WO 2000-JP4683	20000713 <--
	W: AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2378714	AA	20010125	CA 2000-2378714	20000713 <--
	JP 2001081043	A2	20010327	JP 2000-217251	20000713 <--
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	NZ 516466	A	20030228	NZ 2000-516466	20000713 <--
	NO 2002000084	A	20020314	NO 2002-84	20020108 <--
	ZA 2002000347	A	20030115	ZA 2002-347	20020115 <--
PRAI	JP 1999-201887	A	19990715 <--		
	WO 2000-JP4683	W	20000713 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001005380	ICM	A61K0009-52
	ICS	A61K0038-09; A61K0047-12; A61K0047-34; A61P0035-00; A61P0005-24; A61P0013-08; A61P0015-00
	IPCI	A61K0009-52 [ICM,7]; A61K0038-09 [ICS,7]; A61K0047-12 [ICS,7]; A61K0047-34 [ICS,7]; A61P0035-00 [ICS,7]; A61P0005-24 [ICS,7]; A61P0013-08 [ICS,7]; A61P0015-00 [ICS,7]
	IPCR	A61K0009-00 [N,A]; A61K0009-00 [N,C]; A61K0009-16 [I,A]; A61K0009-16 [I,C]
	ECLA	A61K009/16H6D4; A61K009/16H4 <--
CA 2378714	IPCI	A61K0009-52 [ICM,7]; A61P0015-00 [ICS,7]; A61P0035-00 [ICS,7]; A61P0013-08 [ICS,7]; A61K0038-09 [ICS,7]; A61K0047-12 [ICS,7]; A61P0005-24 [ICS,7]; A61K0047-34 [ICS,7] <--
JP 2001081043	IPCI	A61K0038-22 [ICM,7]; A61K0009-52 [ICS,7]; A61K0047-12 [ICS,7]; A61K0047-34 [ICS,7]; A61P0005-02 [ICS,7]; A61P0013-08 [ICS,7]; A61P0015-00 [ICS,7]; A61P0015-18 [ICS,7]; A61P0035-00 [ICS,7] <--
EP 1197208	IPCI	A61K0009-52 [ICM,6]; A61K0038-09 [ICS,6]; A61K0047-12 [ICS,6]; A61K0047-34 [ICS,6]; A61P0035-00 [ICS,6]; A61P0005-24 [ICS,6]; A61P0013-08 [ICS,6]; A61P0015-00 [ICS,6]
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[ICS,7]; A61K0047-34 [ICS,7]; A61P0005-24 [ICS,7];
A61P0013-08 [ICS,7]; A61P0015-00 [ICS,7] <--
NO 2002000084 IPCI A61K0009-52 [ICM,7] <--
ZA 2002000347 IPCI A61K [ICM,7]; A61P [ICS,7] <--

AB The invention relates to sustained release compns. containing a physiol. active substance or its salt, **hydroxynaphthoic acid** or its salt and a **lactic** acid-**glycolic** acid polymer or its salt, wherein the product of the weight-average mol. weight of the **lactic** acid-**glycolic** acid polymer by the amount (<mmol) of the terminal carboxyl group per unit mass (g) of the **lactic** acid-**glycolic** acid polymer is from 1,200,000 to 3,000,000 (inclusive); and drugs, etc. containing these sustained release compns.

ST sustained release **hydroxynaphthoic acid** glycolic copolymer; LHRH deriv sustained release microcapsule

IT Drug delivery systems
(microcapsules, sustained-release; sustained-release compns., process for producing the same and use thereof)

IT Drug bioavailability
(sustained-release compns., process for producing the same and use thereof)

IT Peptides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sustained-release compns., process for producing the same and use thereof)

IT **86-48-6**, 1-**Hydroxy**-2-**naphthoic acid**
92-70-6, 3-**Hydroxy**-2-**naphthoic acid**
9034-40-6D, Lh-rh, derivs. **30440-92-7**, **Hydroxynaphthoic acid** **34346-01-5**, **Lactic** acid-**glycolic** acid copolymer 53714-56-0
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(sustained-release compns., process for producing the same and use thereof)

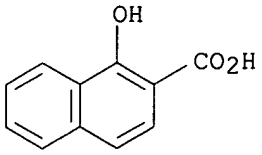
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Takeda Chemical Industries Ltd; JP 08259460 A HCAPLUS
(2) Takeda Chemical Industries Ltd; JP 08259460 A HCAPLUS
(3) Takeda Chemical Industries Ltd; JP 10273447 A HCAPLUS
(4) Takeda Chemical Industries Ltd; JP 11269094 A HCAPLUS
(5) Takeda Chemical Industries Ltd; AU 9644591 A HCAPLUS
(6) Takeda Chemical Industries Ltd; AU 9644591 A HCAPLUS
(7) Takeda Chemical Industries Ltd; AU 9856783 A HCAPLUS
(8) Takeda Chemical Industries Ltd; AU 9918897 A HCAPLUS
(9) Takeda Chemical Industries Ltd; WO 9622786 A1 1996 HCAPLUS
(10) Takeda Chemical Industries Ltd; WO 9622786 A1 1996 HCAPLUS
(11) Takeda Chemical Industries Ltd; WO 9832423 A1 1998 HCAPLUS
(12) Takeda Chemical Industries Ltd; WO 9936099 A1 1999 HCAPLUS

IT **86-48-6**, 1-**Hydroxy**-2-**naphthoic acid**
92-70-6, 3-**Hydroxy**-2-**naphthoic acid**
30440-92-7, **Hydroxynaphthoic acid** **34346-01-5**, **Lactic** acid-**glycolic** acid copolymer
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(sustained-release compns., process for producing the same and use thereof)

RN 86-48-6 HCAPLUS
CN 2-Naphthalenecarboxylic acid, 1-hydroxy- (9CI) (CA INDEX NAME)



RN 92-70-6 HCAPLUS
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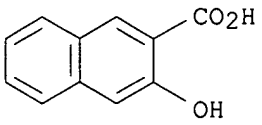
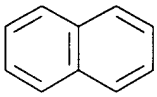


RN 30440-92-7 HCAPLUS
CN Naphthalenecarboxylic acid, hydroxy- (9CI) (CA INDEX NAME)



D1—OH

D1—CO_2H

RN 34346-01-5 HCAPLUS
CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA INDEX NAME)

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CRN 79-14-1
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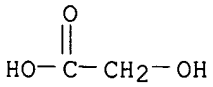
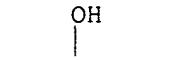


CM 2

CRN 50-21-5
CMF C3 H6 O3



L73 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 1999:468574 HCAPLUS
DN 131:106841
ED Entered STN: 30 Jul 1999
TI Sustained release compositions, process for producing the same and utilization thereof
IN Saikawa, Akira; **Igari, Yasutaka; Hata, Yoshio; Yamamoto, Kazumichio**
PA **Takeda Chemical Industries, Ltd., Japan**
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM A61K0047-30
ICS A61K0047-12; A61K0037-02
CC 63-6 (**Pharmaceuticals**)
Section cross-reference(s): **1**, 2
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9936099	A1	19990722	WO 1999-JP86	19990113
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2316273	AA	19990722	CA 1999-2316273	19990113
	AU 9918897	A1	19990802	AU 1999-18897	19990113
	AU 758596	B2	20030327		
	EP 1048301	A1	20001102	EP 1999-900300	19990113
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	BR 9906903	A	20001212	BR 1999-6903	19990113
	TR 200002059	T2	20010122	TR 2000-200002059	19990113
	NZ 505651	A	20030829	NZ 1999-505651	19990113
	RU 2230550	C2	20040620	RU 2000-121545	19990113
	JP 11269094	A2	19991005	JP 1999-7566	19990114
	US 6740634	B1	20040525	US 2000-582926	20000706
	NO 2000003530	A	20000914	NO 2000-3530	20000707
	HR 2000000471	A1	20001231	HR 2000-471	20000713
	US 2005025826	A1	20050203	US 2004-799320	20040312
PRAI	JP 1998-6412	A	19980116		
	WO 1999-JP86	W	19990113		
	US 2000-582926	A3	20000706		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9936099	ICM	A61K0047-30
	ICS	A61K0047-12; A61K0037-02
	IPCI	A61K0047-30 [ICM,6]; A61K0047-12 [ICS,6]; A61K0037-02 [ICS,6]

	IPCR	A61K0009-16 [I,A]; A61K0009-16 [I,C]; A61K0038-08 [I,C]; A61K0038-09 [I,A]; A61K0047-34 [I,A]; A61K0047-34 [I,C]; A61K0047-48 [I,A]; A61K0047-48 [I,C]
	ECLA	A61K009/16H6D4; A61K038/09; A61K047/34; A61K047/48H4; A61K047/48H4C
CA 2316273	IPCI	A61K0047-30 [ICM,6]; A61K0047-12 [ICS,6]; A61K0038-24 [ICS,6]
	ECLA	A61K009/16H6D4; A61K038/09; A61K047/34; A61K047/48H4; A61K047/48H4C
AU 9918897	ECLA	A61K009/16H6D4; A61K038/09; A61K047/34; A61K047/48H4; A61K047/48H4C
EP 1048301	IPCI	A61K0047-30 [ICM,6]
	IPCR	A61K0009-16 [I,A]; A61K0009-16 [I,C]; A61K0038-08 [I,C]; A61K0038-09 [I,A]; A61K0047-34 [I,A]; A61K0047-34 [I,C]; A61K0047-48 [I,A]; A61K0047-48 [I,C]
	ECLA	A61K009/16H6D4; A61K038/09; A61K047/34; A61K047/48H4; A61K047/48H4C
BR 9906903	IPCI	A61K0038-24 [ICM,7]; A61P0005-06 [ICS,7]; A61P0015-00 [ICS,7]
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NZ 505651	IPCI	A61K0047-30 [ICM,7]; A61K0037-02 [ICS,7]; A61K0047-12 [ICS,7]
	ECLA	A61K009/16H6D4; A61K038/09; A61K047/34; A61K047/48H4; A61K047/48H4C
RU 2230550	IPCI	A61K0009-22 [ICM,7]; A61K0047-12 [ICS,7]; A61K0047-30 [ICS,7]
	ECLA	A61K009/16H6D4; A61K038/09; A61K047/34; A61K047/48H4; A61K047/48H4C
JP 11269094	IPCI	A61K0047-12 [ICM,6]; A61K0009-52 [ICS,6]; A61K0031-00 [ICS,6]; A61K0031-19 [ICS,6]; A61K0038-22 [ICS,6]
US 6740634	IPCI	A61K0038-00 [ICM,7]
	IPCR	A61K0009-16 [I,A]; A61K0009-16 [I,C]; A61K0038-08 [I,C]; A61K0038-09 [I,A]; A61K0047-34 [I,A]; A61K0047-34 [I,C]; A61K0047-48 [I,A]; A61K0047-48 [I,C]
	NCL	514/002.000; 424/468.000; 424/486.000; 530/313.000; 530/399.000
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NO 2000003530	IPCI	A61K0047-12 [ICM,7]; A61K0047-30 [ICS,7]
	ECLA	A61K009/16H6D4; A61K038/09; A61K047/34; A61K047/48H4; A61K047/48H4C
HR 2000000471	IPCI	A61K0047-30 [ICM,7]; A61K0047-12 [ICS,7]; A61K0038-24 [ICS,7]
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US 2005025826	IPCI	A61K0009-00 [ICM,7]; A61K0009-22 [ICS,7]; A61K0009-50 [ICS,7]; A61K0031-19 [ICS,7]
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	NCL	424/468.000
	ECLA	A61K009/16H6D4; A61K038/09; A61K047/34; A61K047/48H4C

OS MARPAT 131:106841

AB The invention relates to sustained release compns. containing a physiol. active substance [peptide A] or its salt, **hydroxynaphthoic**

acid or its salt and a biodegradable polymer or its salt; and drugs, etc. containing these compns.

ST sustained release capsule peptide A; **hydroxynaphthoic acid** sustained release capsule peptide; biodegradable polymer sustained release capsule peptide

IT Prostate gland
(benign hyperplasia; sustained release compns., process for producing the same and utilization thereof)

IT Polymers, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(biodegradable; sustained release compns., process for producing the same and utilization thereof)

IT Drug delivery systems
(capsules, sustained-release; sustained release compns., process for producing the same and utilization thereof)

IT Development, nonmammalian postembryonic
(early puberty; sustained release compns., process for producing the same and utilization thereof)

IT Uterus, disease
(endometriosis; sustained release compns., process for producing the same and utilization thereof)

IT Drug delivery systems
(injections, sustained release; sustained release compns., process for producing the same and utilization thereof)

IT Antitumor agents
(mammary gland; sustained release compns., process for producing the same and utilization thereof)

IT Uterus, disease
(metrofibroma; sustained release compns., process for producing the same and utilization thereof)

IT Drug delivery systems
(microcapsules, sustained-release; sustained release compns., process for producing the same and utilization thereof)

IT Mammary gland
Mammary gland
Prostate gland
Prostate gland
(neoplasm, inhibitors; sustained release compns., process for producing the same and utilization thereof)

IT Antitumor agents
(prostate gland; sustained release compns., process for producing the same and utilization thereof)

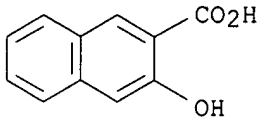
IT Contraceptives
Menstrual disorder
(sustained release compns., process for producing the same and utilization thereof)

IT Drug delivery systems
(sustained-release; sustained release compns., process for producing the same and utilization thereof)

IT **92-70-6**, 3-**Hydroxy**-2-**naphthoic acid**
9034-40-6, Lh-rh 26100-51-6, DL-Lactic acid polymer **30440-92-7**
, **Hydroxynaphthoic acid 34346-01-5**,
Glycolic acid-**lactic** acid copolymer 88793-81-1
168395-24-2 230638-75-2
RL: PEP (Physical, engineering or chemical process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(sustained release compns., process for producing the same and utilization thereof)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE
(1) Takeda Chemical Industries Ltd; EP 889722 A2 HCAPLUS
(2) Takeda Chemical Industries Ltd; WO 9622786 A1 HCAPLUS
(3) Takeda Chemical Industries Ltd; AU 9644591 A1 HCAPLUS
(4) Takeda Chemical Industries Ltd; AU 9720432 A1 HCAPLUS
(5) Takeda Chemical Industries Ltd; WO 9735563 A2 HCAPLUS
(6) Takeda Chemical Industries Ltd; JP 08259460 A2 1996 HCAPLUS
(7) Takeda Chemical Industries Ltd; JP 09315997 A2 1997 HCAPLUS
IT **92-70-6**, 3-**Hydroxy**-2-**naphthoic acid**
30440-92-7, **Hydroxynaphthoic acid**
34346-01-5, **Glycolic** acid-**lactic** acid
copolymer
RL: PEP (Physical, engineering or chemical process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(sustained release compns., process for producing the same and utilization thereof)
RN 92-70-6 HCAPLUS
CN 2-Naphthalenecarboxylic acid, 3-hydroxy- (9CI) (CA INDEX NAME)



RN 30440-92-7 HCAPLUS
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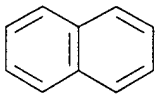

D1—OH

D1—CO_2H

RN 34346-01-5 HCAPLUS
CN Propanoic acid, 2-hydroxy-, polymer with hydroxyacetic acid (9CI) (CA INDEX NAME)

CM 1

CRN 79-14-1
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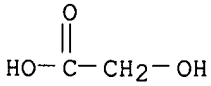
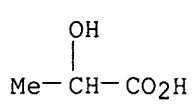


CM 2

CRN 50-21-5
CMF C3 H6 O3



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http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<
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L113 ANSWER 1 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 2005-142542 [15] WPIX
DNC C2005-046378
TI Preparation of controlled release composition by combining an organic phase comprising bioactive agent and polymer with an aqueous phase comprising an organic ion.
DC A28 A96 B07
IN GARY, P C
PA (PRPH-N) PR PHARM
CYC 107
PI WO 2005009356 A2 20050203 (200515)* EN 50 A61K000-00 <--
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE

LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE
DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG
KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ
OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG
UZ VC VN YU ZA ZM ZW

ADT WO 2005009356 A2 WO 2004-US22816 20040715
PRAI US 2003-487663P 20030715
IC ICM **A61K000-00**
AB WO2005009356 A UPAB: 20050303
NOVELTY - Preparation of a controlled release composition (C1) involves combining an organic phase (p1) comprising a bioactive agent (a1) and a polymer (r1), with an aqueous phase (p2) comprising an organic ion (i1).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:
(1) a controlled release composition;
(2) a process for the production of a microparticle; and
(3) an improved process for the production of a microparticle.
USE - For preparation of a controlled release composition (claimed).
ADVANTAGE - The method produces compositions with a high drug load, minimum burst effect upon administration and minimum degradation of the bioactive agent. The method allows use of water soluble peptides and eliminate need to prepare complexed species in independent steps prior to the preparation of the compositions.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: A12-V01; B04-B04C; B04-C01; B04-C03; B04-E01; B04-J01; B04-N02; B05-C05; B07-A04; B07-D03; B10-A09A; B10-A09B; B10-A10; B10-C02; B10-C03; B10-C04C; B10-C04E; B10-D03; B10-E04B; B10-E04D; B10-F02; B10-G02; B10-H02F; **B12-M10A**; B12-M11E
TECH UPTX: 20050303
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: (p1) further comprises a solvent (preferably methylene chloride, ethyl acetate, benzyl alcohol, acetone, acetic acid or propylene carbonate) and a cosolvent (preferably dimethyl sulfoxide, dimethyl formamide, n-methylpyrrolidinone, PEG200, PEG400, methyl alcohol, ethyl alcohol, isopropyl alcohol or benzyl alcohol). (p2) further comprises an emulsifying agent (0.1 - 10 w/w.%) (preferably poly(vinyl alcohol), albumin, lecithin vitamin E-TPGS or polysorbates). (i1) (0.1 - 1000 mM) is selected from carboxylate, sulfate, phosphate, pamoate, dodecylsulfate, trifluoromethyl-p-toluate, dictate, 2-naphthalene sulfonate, 2, 3-naphthalene dicarboxylate, 1-**hydroxy**-2-**naphthoate**, 3-**hydroxy**-2-**naphthoate**, 2-naphthoate, and salicylsalicylate.

TECHNOLOGY FOCUS - POLYMERS - Preferred Components: (r1) is selected from poly(lactide), poly(glycolide), poly(lactide-co-glycolide), poly (lactic acid), poly(glycolic acid), poly(lactic acid-co-glycolic acid), polycaprolactone, polycarbonate, polyesteramide, polyanhydride, poly(amino acid), polyorthoester, polyacetyl, polycyanoacrylate, polyetherester, poly(dioxanone), poly(alkylene alkylate), copolymer of polyethylene glycol and polyorthoester, biodegradable polyurethanes, blend and their copolymer.
Preferred Components: (a1) is selected from protein, nucleic acid, carbohydrate, peptide, LHRH agonist and their synthetic analog, leuprolide, oxytocin, somatostatin and their synthetic analog, small molecule pharmaceutical substance, immunogen, metabolic precursor capable of promoting growth and survival of cell and tissue, antineoplastic agent, hormone, antihistamine, cardiovascular agent, anti-ulcer agent, bronchodilator, vasodilator, central nervous system agent and narcotic antagonist. The protein or peptide is octreotide, oxytocin, insulin,

leuprolide and their synthetic variation. Preferred Composition: (C1) is microparticles and nanoparticles, which are biodegradable. Preferred Method: (p1) and (p2) are combined using an emulsion process (preferably oil-in-water and water-oil-water).

ABEX UPTX: 20050303

ADMINISTRATION - (C1) is administered parenterally (including intravenously or intramuscularly), intradermally, pulmonary, buccally, transdermally or transmucosally (including ophthalmically, vaginally, rectally or intranasally).

EXAMPLE - Microparticle formulations were prepared by an oil-in-water emulsion/solvent extraction method. Poly(lactide-co-glycolide) (PLGA) polymer (MW 24,000, 140 - 180 mg) was dissolved in EtOAc (1000 microL). Octreotide acetate (20 - 60 mg) was dissolved in BnOH (1000 microL) and added to the polymer solution yielding a homogenous organic phase. The resulting organic phase was combined with a 1% polyvinylalcohol (PVA) aqueous phase containing disodium pamoate (10 - 50 mM) to provide an emulsion. The emulsion was collected directly into a 0.3% PVA solvent extraction solution (150 ml) and stirred for four hours to extract EtOAc. Hardened microparticles were collected by filtration, washed with water, air dried and stored at 4degreesC. This resulted in a final octreotide/pamoate ratio of approximately 1 - 1.5 in the microparticle formulation. Product with predictable and elevated drug core loads of 5 - 17.5% could be formed. The composition had consistent stoichiometry for the molar ratio of bioactive agent to organic ion. The relative production of acylated peptide was lower for microparticles made with the organic ion in the aqueous phase than for microparticles made with the use of preformed octreotide-pamoate or octreotide acetate.

L113 ANSWER 2 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 2003-362980 [34] WPIX
DNC C2003-095731
TI Controlled release composition useful for treating prostatic cancer comprises an active substance, optionally **hydroxynaphthoic acid**, and a lactic acid polymer.
DC A96 B07
IN **HATA, Y**; YAMADA, A; **YAMAMOTO, K**
PA (TAKE) **TAKEDA CHEM IND LTD**; (TAKE) **TAKEDA PHARM CO LTD** ; (HATA-I) HATA Y; (YAMA-I) YAMADA A; (YAMA-I) YAMAMOTO K
CYC 100
PI WO 2003002092 A2 20030109 (200334)* EN 52 A61K009-00 <--
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US 2003134800 A1 20030717 (200348) A61K038-07 <--
EP 1330293 A2 20030730 (200350) EN A61P005-06
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
JP 2003206240 A 20030722 (200351) 22 A61K047-12 <--
SK 2003001560 A3 20040608 (200441) A61K009-16 <--
BR 2002010561 A 20040622 (200442) A61P005-06
KR 2004018402 A 20040303 (200443) A61K047-34 <--
AU 2002311631 A1 20030303 (200452) A61K009-00 <--
JP 2004238400 A 20040826 (200456) 31 A61K047-12 <--
CZ 2003003493 A3 20040818 (200457) A61K009-22 <--
EP 1491236 A1 20041229 (200502) EN A61P005-06
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RO SE SI TR

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ZA	2003009152	A	20050126 (200513)	116	A61K000-00	<--
MX	2003011456	A1	20040701 (200545)		A61K009-00	<--
NZ	529969	A	20051028 (200581)		A61K009-16	<--
NO	2003005738	A	20040227 (200612)		A61K047-34	<--

ADT WO 2003002092 A2 WO 2002-JP6527 20020628; US 2003134800 A1 WO 2002-JP6527 20020628, US 2002-182731 20020813; EP 1330293 A2 EP 2002-738838 20020628, WO 2002-JP6527 20020628; JP 2003206240 A JP 2002-189247 20020628; SK 2003001560 A3 WO 2002-JP6527 20020628, SK 2003-1560 20020628; BR 2002010561 A BR 2002-10561 20020628, WO 2002-JP6527 20020628; KR 2004018402 A KR 2003-717129 20031229; AU 2002311631 A1 AU 2002-311631 20020628; JP 2004238400 A Div ex JP 2002-189247 20020628, JP 2004-117981 20040413; CZ 2003003493 A3 WO 2002-JP6527 20020628, CZ 2003-3493 20020628; EP 1491236 A1 Div ex EP 2002-738838 20020628, EP 2004-76939 20020628; CN 1535168 A CN 2002-813061 20020628; HU 2004000378 A2 WO 2002-JP6527 20020628, HU 2004-378 20020628; ZA 2003009152 A ZA 2003-9152 20031125; MX 2003011456 A1 WO 2002-JP6527 20020628, MX 2003-11456 20031210; NZ 529969 A NZ 2002-529969 20020628, WO 2002-JP6527 20020628; NO 2003005738 A NO 2003-5738 20031219

FDT EP 1330293 A2 Based on WO 2003002092; SK 2003001560 A3 Based on WO 2003002092; BR 2002010561 A Based on WO 2003002092; AU 2002311631 A1 Based on WO 2003002092; CZ 2003003493 A3 Based on WO 2003002092; EP 1491236 A1 Div ex EP 1330293; HU 2004000378 A2 Based on WO 2003002092; MX 2003011456 A1 Based on WO 2003002092; NZ 529969 A Based on WO 2003002092

PRAI JP 2001-340993 20011106; JP 2001-199484 20010629

IC ICM **A61K000-00**; **A61K009-00**; **A61K009-16**; **A61K009-22**; **A61K038-07**; **A61K047-12**; **A61K047-34**; A61P005-06

ICS **A61K009-107**; **A61K009-52**; **A61K038-00**; **A61K038-04**; **A61K038-08**; **A61K038-09**; **A61K038-22**; **A61K038-24**; **A61K045-00**; A61P005-00; A61P005-24; A61P013-08; A61P015-00; A61P015-08; A61P015-12; A61P015-18; A61P025-28; A61P035-00; A61P037-00; A61P037-04; A61P043-00; C08K005-13; C08L067-04; C08L077-04

ICA C07K007-23; C08L101-16

AB WO2003002092 A UPAB: 20030529

NOVELTY - A controlled release composition comprises:

(i) an active substance or its salts; and

(ii) a lactic acid polymer or its salts having a weight-average molecular weight of 15000 - 50000 in which the content of polymers having molecular weights of at most 5000 is at most 5 weight%.

The composition optionally comprises **hydroxynaphthoic acid** (iii) or its salts.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a medicine comprising the control release composition; and

(2) preparation of the controlled release composition involving removing a solvent from a mixed solution of (i), (ii) and optionally (iii).

ACTIVITY - Cytostatic; Gynecological; Antitumor; Nootropic; Neuroprotective; Analgesic.

USE - In a medicine for preventing or curing prostatic cancer, prostatic hyperplasia, endometriosis, uterine myoma, uterine fibroma, precocious puberty, dysmenorrhea or breast cancer; preventing recurrence of breast cancer after the operation for premenopausal breast cancer; and as a contraceptive agent (all claimed). For preventing or treating hormone-dependent diseases particularly sex hormone-dependent diseases (preferably sex hormone-dependant cancers (e.g. pituitary tumor, uterine cancer, etc.), amenorrhea, premenstrual syndrome, multiocular ovary

syndrome; Alzheimer disease, immune deficiency and benign or malignant tumor.

ADVANTAGE - The composition contains the active substance in high content and provides stable releasing speed for long period of time by suppressing the initial excess release.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: A05-E02; A12-V01; B04-C03C; B04-J07; B10-C03; B10-C04D; **B12-M10**; B14-H01B; B14-N14; B14-P01B

TECH UPTX: 20030529

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Method: Preparation of the controlled release composition involving mixing and dispersing an aqueous solution of the active substance or its salts into an organic solvent solution containing **hydroxynaphthoic acid** or its salts, and a lactic acid polymer or its salts having a weight-average molecular weight of 15000 to 50000 in which the content of polymers having molecular weights of at most 5000 or is at most 5 (wt.%), then, removing the organic solvent. The salt of (i) is with a free base or acid.

Preferred Component: (i) is active peptide (preferably LH-RH derivative of formula 5-oxo-Pro-His-Trp-Ser-Tyr-Y-Leu-Arg-Pro-Z (I) or its salt (preferably an acetate salt). (iii) is 3-**hydroxy**-2-**naphthoic acid** or 1-**hydroxy**-2-**naphthoic acid**.

Y = DLeu, DAla, DTrp, DSer(tBu), D2Nal or DHis(ImBzl); and

Z = NH-C2H5 or Gly-NH2.

Preferred Composition: The composition comprises (i) in an amount of 3 - 24 (preferably 14 - 24) (w/w.%). The molar ratio of (iii) to (i) is 3:4 - 4:3.

TECHNOLOGY FOCUS - POLYMERS - Preferred Component: (ii) has weight-average molecular weight of 15000 - 40000 (preferably 17000 to 26000). A content of polymers having molecular weights of at most 3000 (preferably at most 1000) or is at most 1.5 (preferably at most 0.1) (wt%).

ABEX UPTX: 20030529

ADMINISTRATION - The composition is administered by injection (claimed). Dosage comprises 0.01 - 10 (preferably 0.05 - 50) mg/kg and administered orally, by injection, muscularly, subcutaneously, permucosally, nasally or rectally.

EXAMPLE - A solution prepared by dissolving DL-lactic acid polymer (144.4 g, weight-average molecular weight 22500) into dichloromethane (111.7 g), and a solution prepared by dissolving 3-**hydroxy**-2-**naphthoic acid** (7.5 g) into dichloromethane (175.1 g) and ethanol (13.5 g), were mixed and controlled to 28.7 degrees C. The portion of solution (274.4 g) was weighed and mixed with an aqueous solution obtained by dissolving an acetate of 5-oxo-Pro-His-Trp-Ser-Tyr-DLeu-Leu-Arg-Pro-NH-C2H5 (peptide A) (24.89 g) into distilled water (23.47 g) and heated to 54.5 degrees C, and stirred for 5 minutes. The solution was cooled to 15 degrees C and poured into 0.1 (wt/weight%) polyvinyl alcohol (25 l). The emulsion was maintained at 15 degrees C for 30 minutes, stirred for 2 hours and 30 minutes, the resulting microcapsules were precipitated and collected, mannitol (15.4 g) was added and then the solution was freeze-dried to give a powder. The recovered weight of the microcapsule powder was (101.6 g) having the peptide A content of (15.88 %) and 3-**hydroxy**-2-**naphthoic acid** content of (2.82 %). The microcapsule (45 mg) was dispersed in dispersion medium (distilled water containing carboxymethylcellulose (0.15 mg), Polysorbate 80 (0.3 mg) and mannitol (15 mg)) and the dispersion was administered by injection to male SD rat subcutaneously in its back. After administration the rat was sacrificed and peptide A content was quantified and divided by

the initial content to give remaining ratio. The remaining ratio (%) of peptide A after 1 day, 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks, 20 weeks and 26 weeks was 92.1, 87.4, 78.1, 64.8, 51.5, 38.7, 11.8 and 2 respectively. The results indicated that the microcapsule allowed release of peptide A at a constant speed for a very long period of time.

L113 ANSWER 3 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 2003-140138 [13] WPIX
DNC C2003-035419
TI New immediate-release pharmaceutical formulation useful e.g. in the treatment of cardiac arrhythmias, comprises 9-oxa-3,7-diazabicyclo(3.3.1) compounds or their salts, and diluent or carrier.
DC A96 B02
IN HOVDAL, C; LUNDGREN, A
PA (ASTR) ASTRAZENECA AB; (HOVD-I) HOVDAL C; (LUND-I) LUNDGREN A
CYC 101
PI WO 2002083689 A1 20021024 (200313)* EN 87 C07D498-08
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
NO 2003004529 A 20031208 (200404) A61K009-10 <--
EP 1389212 A1 20040218 (200413) EN C07D498-08
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
HU 2003003486 A2 20040128 (200415) C07D498-08
SK 2003001256 A3 20040302 (200419) C07D498-08
BR 2002008828 A 20040309 (200420) C07D498-08
KR 2003088498 A 20031119 (200420) A61K031-5386 <--
CZ 2003002774 A3 20040114 (200429) C07D498-08
AU 2002253750 A1 20021028 (200433) C07D498-08
CN 1514839 A 20040721 (200468) C07D498-08
MX 2003009209 A1 20040201 (200473) A61K031-5386 <--
JP 2005500262 W 20050106 (200505) 127 A61K031-5386 <--
US 2005037067 A1 20050217 (200514) A61K009-20 <--
NZ 528561 A 20050324 (200523) C07D498-08
ZA 2003007756 A 20050330 (200527) 94 C07D000-00
ADT WO 2002083689 A1 WO 2002-SE726 20020412; NO 2003004529 A WO 2002-SE726 20020412, NO 2003-4529 20031009; EP 1389212 A1 EP 2002-723011 20020412, WO 2002-SE726 20020412; HU 2003003486 A2 WO 2002-SE726 20020412, HU 2003-3486 20020412; SK 2003001256 A3 WO 2002-SE726 20020412, SK 2003-1256 20020412; BR 2002008828 A BR 2002-8828 20020412, WO 2002-SE726 20020412; KR 2003088498 A KR 2003-713299 20031010; CZ 2003002774 A3 WO 2002-SE726 20020412, CZ 2003-2774 20020412; AU 2002253750 A1 AU 2002-253750 20020412; CN 1514839 A CN 2002-811636 20020412; MX 2003009209 A1 WO 2002-SE726 20020412, MX 2003-9209 20031009; JP 2005500262 W JP 2002-581444 20020412, WO 2002-SE726 20020412; US 2005037067 A1 WO 2002-SE726 20020412, US 2004-474584 20040311; NZ 528561 A NZ 2002-528561 20020412, WO 2002-SE726 20020412; ZA 2003007756 A ZA 2003-7756 20031003
FDT EP 1389212 A1 Based on WO 2002083689; HU 2003003486 A2 Based on WO 2002083689; SK 2003001256 A3 Based on WO 2002083689; BR 2002008828 A Based on WO 2002083689; CZ 2003002774 A3 Based on WO 2002083689; AU 2002253750 A1 Based on WO 2002083689; MX 2003009209 A1 Based on WO 2002083689; JP 2005500262 W Based on WO 2002083689; NZ 528561 A Based on WO 2002083689
PRAI SE 2001-1329 20010412
IC ICM **A61K009-10**; **A61K009-20**; **A61K031-5386**; C07D000-00; C07D498-08

ICS **A61K009-08; A61K009-19; A61K009-48; A61K047-02; A61K047-10; A61K047-12; A61K047-26; A61K047-32; A61K047-34; A61K047-36; A61K047-38;** A61P009-06

AB WO 200283689 A UPAB: 20030224
NOVELTY - An immediate-release pharmaceutical formulation (I) comprising 9-oxa-3,7-diazabicyclo(3.3.1) compounds or their salts as active ingredient, and diluent or carrier, is new.

DETAILED DESCRIPTION - An immediate-release pharmaceutical formulation (I) comprising 9-oxa-3,7-diazabicyclo(3.3.1) compounds or their salts (as active ingredient) selected from 4-((3-(7-(3,3-dimethyl-2-oxobutyl)-9-oxa-3,7-diazabicyclo(3.3.1)-non-3-yl)propyl)amino)benzonitrile (A), tert-butyl 2-(7-(3-(4-cyanoanilino)propyl)-9-oxa-3,7-diazabicyclo(3.3.1)-non-3-yl)ethylcarbamate (B), tert-butyl 2-(7-(4-(4-cyanophenyl)butyl)-9-oxa-3,7-diazabicyclo(3.3.1)-non-3-yl)ethylcarbamate (C), tert-butyl 2-(7-((2S)-3-(4-cyanophenoxy)-2-hydroxypropyl)-9-oxa-3,7-diazabicyclo(3.3.1)-non-3-yl)ethylcarbamate (D) or their salts, and diluent or carrier, is new.

An INDEPENDENT CLAIM is also included for a process for the preparation of (I) comprising bringing the active ingredient into association with the diluent or carrier using wet or dry granulation and/or direct compression/compaction process.

ACTIVITY - Antiarrhythmic; Cardiant; Vasotropic; Anticoagulant; Thrombolytic.

MECHANISM OF ACTION - None given.

USE - (I) are used in the manufacture of a medicament for the prophylaxis or treatment of an arrhythmia e.g. atrial or ventricular arrhythmia, atrial fibrillation (e.g. atrial flutter)) (claimed), cardiovascular disorder, ischemic heart disease, sudden heart attack, myocardial infarction, heart failure, cardiac surgery, or thromboembolic events. Also, (I) are useful in foods or pharmaceuticals.

ADVANTAGE - (I) can be administered directly. (I) is stable during storage and easy to administer. (I) releases the active ingredient in an amount of at least 70 (preferably at least 80)% within 4 (preferably within 1) hour(s) or within 30 minutes.

Dwg.0/22

FS CPI

FA AB; DCN

MC CPI: A12-V01; B04-C02A; B04-C02B; B04-C03A; B04-C03C; B05-A01B; B05-B02A3; B05-B02C; B05-C04; B06-E03; B06-E05; B07-A02B; B10-A07; B10-C02; B10-C04; B10-C04D; B10-E04C; B11-C09; B12-M05; B12-M06; B12-M09; **B12-M10C**; B14-F01; B14-F02; B14-F02D; B14-F04

TECH UPTX: 20030224
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Formulation: (I) is in the form of an immediate release tablet comprising the active ingredient, diluent, carrier and optionally at least one additional excipient (preferably lubricant, glidant, binder and/or disintegrant).
(I) contains (w/w.%) diluent/carrier (up to 40, preferably up to 30, especially up to 20, particularly up to 10), excipient (up to 5, preferably up to 10).
When (I) comprises (A) either as the free base, para-toluenesulfonic acid salt, or benzene sulfonic acid salt and an aqueous carrier along with ethanol as sole additional excipient, then the ethanol is present in an amount of not more than 10 w/w.% of the content of carrier.
(I) is in the form of an aqueous solution.
The solubility of the active ingredient in the aqueous solution is at least 1 (preferably at least 2) mg/ml.
(I) can be provided in the form of a concentrate.
The concentrate is used for preparation of the formulation by adding further diluent or carrier prior to administration.

(I) can be a solid or a freeze-dried pharmaceutical composition.
Preferred Method: The diluent or carrier is added to a mixture of a acid and base.
The process further involves removal of diluent or carrier, by concentrating (preferably evaporating under reduced pressure) the resultant formulation.
The diluent or carrier is removed by evaporation (under reduced pressure), spray drying or freeze-drying.
Preferred Components: The excipient also comprises antimicrobial preservatives, tonicity modifiers, pH adjusting agents, pH controlling agents, surfactants, cosolvents and/or antioxidants.
The active ingredient is water-soluble.

TECHNOLOGY FOCUS - POLYMERS - Preferred Components: The diluent or carrier is an aqueous carrier.
The diluent or carrier is microcrystalline cellulose or silicified microcrystalline cellulose (preferably microcrystalline cellulose).
The binder is polyvinylpyrrolidone, microcrystalline cellulose, polyethylene glycol, polyethylene oxide, hydroxypropylmethylcellulose of a low molecular weight, a methylenecellulose of a low molecular weight, hydroxypropylcellulose of a low molecular weight, hydroxyethylcellulose of a low molecular weight or sodium carboxymethyl cellulose of a low molecular weight (preferably polyvinyl pyrrolidone or hydroxypropylmethylcellulose of a low molecular weight).
The disintegrant is sodium starch glycolate, crosslinked polyvinylpyrrolidone, crosslinked carboxymethyl cellulose or an alginate (preferably sodium starch glycolate, crosslinked polyvinylpyrrolidone or crosslinked sodium carboxymethyl cellulose).

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The tonicity modifier is sodium chloride, mannitol or glucose (preferably mannitol).
The pH controlling agent is tartaric acid, acetic acid or citric acid.
The diluent or carrier is lactose, mannitol, sorbitol, maize starch, potato starch, rice starch or glucose.
The binder and disintegrant is maize starch, potato starch or rice starch.
The cosolvent is ethanol, polyethylene glycol or hydroxypropyl-beta-cyclodextrin.
TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Components: The lubricant is magnesium stearate, stearic acid, calcium stearate, stearyl alcohol or sodium stearyl fumarate (preferably magnesium stearate or sodium stearyl fumarate).
The lubricant is talc or colloidal silica.
The pH adjusting agent is HCl or NaOH.
The diluent or carrier is monobasic calcium phosphate, dibasic calcium phosphate (dihydrate or anhydrate), tribasic calcium phosphate, calcium lactate or calcium carbonate (preferably diabasic calcium phosphate (dihydrate or anhydrate)).

ABEX UPTX: 20030224

SPECIFIC COMPOUNDS - 1-**Hydroxy**-2-**naphthoic acid**, hydroxybenzenesulfonic acid, benzenesulfonic acid, toluene-sulfonic acid, naphthalene sulfonic acid, naphthalenedisulfonic acid, mesitylene-sulfonic acid, methane sulfonic acid, tartaric acid, succinic acid, citric acid, acetic acid, hippuric acid, benzoic acid, hydrochloric acid and hydrobromic acid are specifically claimed as the salts of (A).
Lysine monohydrochloride, pamoic acid, terephthalic acid, methanesulfonic acid, tartaric acid, succinic acid, citric acid, acetic acid, hippuric acid, benzoic acid, hydrochloric acid or hydrobromic acid are specifically claimed as the salts of (D).
Methanesulfonic acid, tartaric acid, succinic acid, citric acid, acetic

acid, hippuric acid, hydrochloric acid and hydrobromic acid are specifically claimed as the salts of (B) and (C) respectively.

ADMINISTRATION - (I) is administered perorally in the form a tablet, capsule, or liquid dosage form, parenterally (including subcutaneously, intravenously, intraarterially, transdermally, intranasally, intrabuccally, intracutaneously, intramuscularly, intralipomateously, intraperitoneally) rectally or sublingually, topically or by inhalation (claimed) in a dosage of 10 - 2000 (preferably 50 - 1000) mg.

EXAMPLE - An aqueous formulation was prepared by dissolving 4-((3-(7-(3,3-dimethyl-2-oxobutyl)-9-oxa-3,7-diazabicyclo(3.3.1)-non-3-yl)propyl)amino)benzonitrile (A; 60 micromol) in tartaric acid (60 micromol), water was added to about 90% of the final volume. The pH was checked and adjusted to 4 by addition of aqueous sodium hydroxide (q.s). The water (1 ml) was added to the final volume. The composition was orally administered to rats in a 14 day toxicity study at a dosage of 420 micromol/kg, and obtaining a plasma concentration of 5.4 - 8.4 microM after 1 hour.

L113 ANSWER 4 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 2003-058393 [05] WPIX
DNC C2003-014888
TI Medicinal solution comprises nonpeptidic active agent, organic acid and biocompatible organic solvent.
DC A96 B05
IN AKIYAMA, Y; MATSUMOTO, Y; YAMAGATA, Y
PA (TAKE) **TAKEDA CHEM IND LTD**; (AKIY-I) AKIYAMA Y; (MATS-I) MATSUMOTO Y; (YAMA-I) YAMAGATA Y
CYC 100
PI WO 2002078669 A1 20021010 (200305)* JA 91 A61K009-08 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
JP 2002356446 A 20021213 (200311) 30 A61K047-12 <--
EP 1374855 A1 20040102 (200409) EN A61K009-08 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
AU 2002243003 A1 20021015 (200432) A61K009-08 <--
US 2004116522 A1 20040617 (200440) A61K031-205 <--
ADT WO 2002078669 A1 WO 2002-JP3145 20020329; JP 2002356446 A JP 2002-94496 20020329; EP 1374855 A1 EP 2002-708717 20020329, WO 2002-JP3145 20020329; AU 2002243003 A1 AU 2002-243003 20020329; US 2004116522 A1 WO 2002-JP3145 20020329, US 2003-473189 20030925
FDT EP 1374855 A1 Based on WO 2002078669; AU 2002243003 A1 Based on WO 2002078669
PRAI JP 2001-99578 20010330
IC ICM **A61K009-08; A61K031-205; A61K047-12**
ICS **A61K009-48; A61K047-20; A61K047-34**
AB WO 200278669 A UPAB: 20030121
NOVELTY - Medicinal solutions comprise a nonpeptidic active agent, an organic acid and a biocompatible organic solvent.
ACTIVITY - None given.
MECHANISM OF ACTION - Gonadotropin releasing hormone agonist; Somatostatin receptor agonist.
USE - As solutions for administering non-peptidic pharmaceuticals such as gonadotropin releasing hormone agonists and somatostatin receptor

agonists.
ADVANTAGE - Active substance is dissolved at high concentrations and have good bioavailability.
Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: A12-V01; B04-C03C; B06-F03; B10-A10; B10-C03; B10-C04D; B12-M07
TECH UPTX: 20030121
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Solution: Solution comprises (a) at least 5 weight% nonpeptidic active agent having a molecular weight of less than 1000; (b) 1-40 weight% lower aliphatic acid, aliphatic hydroxycarboxylic acid (preferably lactic acid) or aromatic organic acid (preferably salicylic acid, 1-**hydroxy**-2-**naphthoic acid** or 3-**hydroxy**-2-**naphthoic acid**); and (c) polyethylene glycol or its aliphatic acid ester or dimethylsulfoxide. Composition is formulated for non-oral (preferably injection) or oral use.
ABEX UPTX: 20030121
EXAMPLE - A medicinal solution comprised 5-(N-benzyl-N-methylaminomethyl)-1-(2,6-difluorobenzyl)-6-(4-(3-methoxyureido)phenyl)-3-phenylthieno(2,3-d)pyrimidine-2,4 (1H,3H)-dione (I) (1200 mg), salicylic acid (372.6 mg) and dimethylsulfoxide (2 ml). The solution (200 mul) was administered subcutaneously to SD rats and gave blood (I) concentrations of 6.0, 19.9, 12.0, and 9.0 ng/ml after 2, 7, 14 and 21 hours respectively.

L113 ANSWER 5 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 2001-168445 [17] WPIX
DNC C2001-050282
TI Sustained release composition e.g. for peptides comprises active substance, **hydroxynaphthoic acid** and lactic acid-glycolic acid polymer.
DC A96 B07
IN **HATA, Y; IGARI, Y; YAMAMOTO, K**
PA (TAKE) **TAKEDA CHEM IND LTD**
CYC 94
PI WO 2001005380 A1 20010125 (200117)* JA 49 A61K009-52 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AU AZ BA BB BG BR BY BZ CA CN CR CU CZ DM DZ EE GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT LV MA MD MG MK MN MX MZ NO NZ PL RO RU SG SI SK TJ TM TR TT UA US UZ VN YU ZA
JP 2001081043 A 20010327 (200122) 18 A61K038-22 <--
AU 2000058530 A 20010205 (200128) A61K009-52 <--
CZ 2002000114 A3 20020417 (200231) A61K009-52 <--
NO 2002000084 A 20020314 (200232) A61K000-00 <--
EP 1197208 A1 20020417 (200233) EN A61K009-52 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
BR 2000012400 A 20020521 (200238) A61K009-52 <--
SK 2002000034 A3 20020509 (200239) A61K009-52 <--
KR 2002012312 A 20020215 (200257) A61K047-34 <--
CN 1361685 A 20020731 (200279) A61K009-52 <--
JP 2001510437 X 20030204 (200320) A61K009-52 <--
HU 2002002880 A2 20030128 (200323) A61K009-52 <--
NZ 516466 A 20030228 (200323) A61K009-52 <--
ZA 2002000347 A 20030326 (200327) 76 A61K000-00 <--
MX 2002000461 A1 20020801 (200367) A61K038-09 <--
ADT WO 2001005380 A1 WO 2000-JP4683 20000713; JP 2001081043 A JP 2000-217251 20000713; AU 2000058530 A AU 2000-58530 20000713; CZ 2002000114 A3 WO 2000-JP4683 20000713, CZ 2002-114 20000713; NO 2002000084 A WO 2000-JP4683

20000713, NO 2002-84 20020108; EP 1197208 A1 EP 2000-944418 20000713, WO 2000-JP4683 20000713; BR 2000012400 A BR 2000-12400 20000713, WO 2000-JP4683 20000713; SK 2002000034 A3 WO 2000-JP4683 20000713, SK 2002-34 20000713; KR 2002012312 A KR 2002-700546 20020114; CN 1361685 A CN 2000-810405 20000713; JP 2001510437 X WO 2000-JP4683 20000713, JP 2001-510437 20000713; HU 2002002880 A2 WO 2000-JP4683 20000713, HU 2002-2880 20000713; NZ 516466 A NZ 2000-516466 20000713, WO 2000-JP4683 20000713; ZA 2002000347 A ZA 2002-347 20020115; MX 2002000461 A1 WO 2000-JP4683 20000713, MX 2002-461 20020114

FDT AU 2000058530 A Based on WO 2001005380; CZ 2002000114 A3 Based on WO 2001005380; EP 1197208 A1 Based on WO 2001005380; BR 2000012400 A Based on WO 2001005380; SK 2002000034 A3 Based on WO 2001005380; JP 2001510437 X Based on WO 2001005380; HU 2002002880 A2 Based on WO 2001005380; NZ 516466 A Based on WO 2001005380; MX 2002000461 A1 Based on WO 2001005380

PRAI JP 1999-201887 19990715

IC ICM **A61K000-00**; **A61K009-52**; **A61K038-09**; **A61K038-22**; **A61K047-34**

ICS **A61K038-00**; **A61K047-12**; A61P005-02; A61P005-24; A61P013-08; A61P015-00; A61P015-18; A61P035-00

AB WO 200105380 A UPAB: 20010328

NOVELTY - Sustained release composition comprises:

(a) physiologically active substance;

(b) **hydroxynaphthoic acid**; and

(c) a lactic acid-glycolic acid polymer.

DETAILED DESCRIPTION - Sustained release composition comprises:

(a) physiologically active substance or its salt;

(b) **hydroxynaphthoic acid** or its salt; and

(c) a lactic acid-glycolic acid polymer or its salt having a weight-average molecular weight by the amount (micro mol) of the terminal carboxyl group per unit mass (g) of the lactic acid-glycolic acid polymer of 1200000-3000000.

ACTIVITY - Cytostatic;

USE - As a sustained release composition especially an injection for peptides such as luteinizing hormone releasing hormone (LH-RH) compounds for treating and preventing e.g. prostate cancer, prostatic hypertrophy, uterine cancer, myometrium cancer, pubescent disturbances, uterine fibrosarcoma, and breast cancer.

ADVANTAGE - Gives sustained release over a long period of time e.g. several months.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: A05-E02; A12-V01; B04-C01B; B04-C03D; B04-J07; B10-C04A; **B12-M10A**; B14-H01; B14-N14

TECH UPTX: 20010328

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: Composition comprises:

(i) a peptide or a luteinizing hormone releasing hormone (LH-RH) compound (preferably of formula 5-oxo-Pro-His-Trp-Ser-Tyr-Y-Leu-Arg-Pro-Z (I);

(ii) 3-**hydroxy**-2-**naphthoic acid** or preferably 1-**hydroxy**-2-**naphthoic acid**; and

(iii) lactic acid-glycolic acid polymer having a mol ratio of 100/0-40/60 (preferably 100/0) % and a weight-average molecular weight of 3000-100000 (preferably 20000-50000).

Y = DLeu, DAla, DTrp, DSer(tBu), D2Nal or DHis(ImBzl); and

Z = NHEt or Gly-NH2.

ABEX UPTX: 20010328

ADMINISTRATION - Dosage is 0.01-10 (preferably 0.05-5) mg/kg/day a.i.

EXAMPLE - 5-Oxo-Pro-His-Trp-Ser-Tyr-DLeu-Leu-Arg-Pro-NHEt (Ia) (1.2 g) in

water (1.2 ml) and DL-lactose polymer (molecular weight 40600; terminal carboxy groups 52.7 mu mol/g) and 1-**hydroxy**-2-**naphthoic acid** (0.18 g) in dichloromethane (8.25 ml) and ethanol (0.45 ml) were homogenized to give a water in oil emulsion. The emulsion was homogenized with 0.1 % (w/w) polyvinyl alcohol in water (1200 ml) at 7000 rpm for 3 hours to give a water-in oil-in water emulsion. The emulsion was used to prepare a macrogel containing 18.7 % (Ia). A solution containing the macrogel (45 mg) was injected into SD rats and the % (Ia) remaining after 1 day, 2 weeks, 8 weeks, 16 weeks and 26 weeks was 92.9, 74.6, 31.6, 24.5 and 12.6 % respectively.

L113 ANSWER 6 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 1999-444329 [37] WPIX
DNC C1999-130900
TI Slow-release composition, especially containing luteinising hormone release hormone for treating breast, prostate or uterine cancer, as a contraceptive etc..
DC A23 A35 A96 B04 B07 P81
IN **HATA, Y; IGARI, Y;** SAIKAWA, A; **YAMAMOTO, K**
PA (TAKE) **TAKEDA CHEM IND LTD**; (HATA-I) HATA Y; (IGAR-I) IGARI Y; (SAIK-I) SAIKAWA A; (YAMA-I) YAMAMOTO K
CYC 84
PI WO 9936099 A1 19990722 (199937)* JA 57 A61K047-30 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE GD GE HR HU ID IL IN IS JP KE KG KR KZ LC LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK SL TJ TM TR TT UA US UZ VN YU
JP 11269094 A 19991005 (199953) 20 A61K047-12 <--
AU 9918897 A 19990802 (199954)
EP 1048301 A1 20001102 (200056) EN A61K047-30 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
NO 2000003530 A 20000914 (200058) A61K047-12 <--
CZ 2000002470 A3 20001011 (200060) A61K047-30 <--
BR 9906903 A 20001212 (200102) A61K038-24 <--
SK 2000001027 A3 20010118 (200108) A61K047-30 <--
CN 1288387 A 20010321 (200137) A61K047-30 <--
HU 2001000221 A2 20010628 (200143) A61K047-30 <--
KR 2001033949 A 20010425 (200164) A61K038-24 <--
MX 2000006641 A1 20010201 (200168) A61K037-02 <--
JP 2000539871 X 20020924 (200278) A61K047-30 <--
AU 758596 B 20030327 (200330) A61K047-30 <--
NZ 505651 A 20030829 (200365) A61K047-30 <--
US 6740634 B1 20040525 (200435) A61K038-00 <--
RU 2230550 C2 20040620 (200446) A61K009-22 <--
US 2005025826 A1 20050203 (200511) A61K009-00 <--
IN 2000000096 P2 20050318 (200575) EN A61K047-30 <--
ADT WO 9936099 A1 WO 1999-JP86 19990113; JP 11269094 A JP 1999-7566 19990114; AU 9918897 A AU 1999-18897 19990113; EP 1048301 A1 EP 1999-900300 19990113, WO 1999-JP86 19990113; NO 2000003530 A WO 1999-JP86 19990113, NO 2000-3530 20000707; CZ 2000002470 A3 WO 1999-JP86 19990113, CZ 2000-2470 19990113; BR 9906903 A BR 1999-6903 19990113, WO 1999-JP86 19990113; SK 2000001027 A3 WO 1999-JP86 19990113, SK 2000-1027 19990113; CN 1288387 A CN 1999-802114 19990113; HU 2001000221 A2 WO 1999-JP86 19990113, HU 2001-221 19990113; KR 2001033949 A KR 2000-707533 20000707; MX 2000006641 A1 MX 2000-6641 20000705; JP 2000539871 X WO 1999-JP86 19990113, JP 2000-539871 19990113; AU 758596 B AU 1999-18897 19990113; NZ 505651 A NZ 1999-505651 19990113, WO 1999-JP86 19990113; US 6740634 B1 WO 1999-JP86 19990113, US 2000-582926 20000706; RU 2230550 C2 WO 1999-JP86 19990113, RU 2000-121545 19990113; US 2005025826 A1 Div ex WO 1999-JP86 19990113, Div

ex US 2000-582926 20000705, US 2004-799320 20040312; IN 2000000096 P2 WO 1999-JP86 19990113, IN 2000-KN96 20000426

FDT AU 9918897 A Based on WO 9936099; EP 1048301 A1 Based on WO 9936099; CZ 2000002470 A3 Based on WO 9936099; BR 9906903 A Based on WO 9936099; HU 2001000221 A2 Based on WO 9936099; JP 2000539871 X Based on WO 9936099; AU 758596 B Previous Publ. AU 9918897, Based on WO 9936099; NZ 505651 A Based on WO 9936099; US 6740634 B1 Based on WO 9936099; RU 2230550 C2 Based on WO 9936099; US 2005025826 A1 Div ex US 6740634

PRAI JP 1998-6412 19980116

IC ICM **A61K009-00**; **A61K009-22**; **A61K037-02**; **A61K038-00**; **A61K038-24**; **A61K047-12**; **A61K047-30**
ICS **A61K009-50**; **A61K009-52**; **A61K031-00**; **A61K031-19**; **A61K038-09**; **A61K038-22**; A61P005-06; A61P013-08; A61P015-00; A61P035-00; A61P039-00; G02F001-35

AB WO 9936099 A UPAB: 20011203

NOVELTY - A slow-release composition comprises a physiologically active material or its salt, a **hydroxynaphthoic acid** or its salt and a biodegradable polymer or its salt.

USE - The composition containing LH-RH derivative is useful as a contraceptive or for preventing and treating prostate cancer, prostate hypertrophy, endometriosis, fibroids or myoma of the uterus, menstrual difficulties or breast cancer (claimed), polycystic ovary, cancer of the hypophysis or amennorhoea, in humans and other animals.

ADVANTAGE - The composition has low toxicity.

Dwg.0/0

FS CPI GMPI

FA AB; DCN

MC CPI: A05-E02; A09-A07; A12-V; A12-V01; B04-C03D; B04-J07; B10-C03; B10-C04D; **B12-M10A**; B12-M11E

TECH UPTX: 19990914

TECHNOLOGY FOCUS - POLYMERS - The polymer is a polymer of an alpha-hydroxyacid, especially lactic acid-glycollic acid.

TECHNOLOGY FOCUS - PHARMACEUTICALS - The active material is a peptide, especially an LH-RH derivative.

ABEX UPTX: 19990914

SPECIFIC COMPOUNDS - The acid is 3-**hydroxy**-2-**naphthoic acid**.

ADMINSTRATION - Dosage is 0.05-50 mg/kg of active component every 1-6 months in humans. Administration is orally, i.m., s.c., through the mucous membrane of the target organ etc.

EXAMPLE - N-(S)-tetrahydrofur-2-oyl-Gly-D2Nal-D4ClPhe-D3Pal-Ser-NMeTyr-DLys(Nic)-Leu-Lys(Nisp)-Pro-DAlaNH2 (peptide A) acetate (1800mg), 3-**hydroxy**-2-**naphthoic acid** (173 mg) and lactate-glycollate copolymer (2g) (lactate/glycollate 50/50 mole %, of Mw 10100, Mn 5670, 268.8 micromole/g carboxy) were dissolved in ethanol (2 ml) and CH2Cl2 (6 ml), introduced at 18 degreesC into 0.1 % (w/w) polyvinyl alcohol solution (900 ml) containing 5% mannitol, and formed into an emulsion by stirring at 7000 rpm. The emulsion was stirred to allow the organic solvents to escape (or dispersed in water). The oil phase was solidified and sieved (75 micron mesh) then centrifuged to collect the microcapsules. These were suspended in water, re-centrifuged, dispersed in mannitol (250 mg) and a small amount of water, and freeze dried. The recovery rate of material in microcapsules, apart from the mannitol, was 76 %, content of peptide A was 34.7 %, and ratio of the naphthoic acid to peptide was 1.19. These microcapsules were suspended in

water containing carboxymethyl cellulose, polysorbate 80 and mannitol as suspending agents, and injected subcutaneously into the back of rats. The amount of peptide remaining was 70 % after the first day, 31 % after the first week and 9 % after the third week.

=> => d his

(FILE 'HOME' ENTERED AT 06:51:45 ON 14 MAR 2006)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 06:52:08 ON 14 MAR 2006
L1 1 S (WO2000-JP4683 OR JP99-201887)/AP,PRN
E IGARI/AU
L2 81 S E77,E78
E YASUTAKA/AU
E HATA/AU
E HATA Y/AU
L3 92 S E3,E4,E40
E YOSHIO/AU
L4 7 S E3,E17
E YAMAMOTO/AU
L5 5 S E3
E YAMAMOTO K/AU
L6 1597 S E3-E8,E143,E144,E145
E KAZUMICHI/AU
E TAKEDA/PA,CS
L7 14786 S TAKEDA?/PA,CS
SEL RN L1

FILE 'REGISTRY' ENTERED AT 06:56:03 ON 14 MAR 2006
L8 6 S E1-E6
L9 3 S L8 AND C6-C6/ES
E C11H8O3/MF
L10 95 S E3 AND C6-C6/ES AND 2/NR
L11 69 S L10 AND HYDROXY
L12 25 S L11 AND ACID
L13 19 S L12 NOT (LABELED OR (D OR T)/ELS OR 11C# OR 13C# OR 14C# OR C
L14 19 S L9,L13
L15 1 S L8 AND PMS/CI
L16 3 S (D-LACTIC ACID OR DL-LACTIC ACID OR L-LACTIC ACID)/CN
L17 7 S C6H8O4/MF AND OC2OC2/ES AND 2 5 DIONE AND 3 6 DIMETHYL
L18 5 S L17 NOT D/ELS
L19 8 S L16,L18
L20 1 S GLYCOLIC ACID/CN
L21 1 S C4H4O4/MF AND OC2OC2/ES AND 2 5 DIONE
L22 2 S L20,L21
SEL RN
L23 2844 S E1-E2/CRN
SEL RN L19
L24 5207 S E3-E10/CRN
L25 486 S L23 AND L24
L26 17 S L25 AND 2/NC
L27 38 S L25 AND SALT
L28 12 S L27 AND 2/NR
L29 7 S L28 AND NA
L30 1 S L29 AND 3/NC
L31 18 S L26,L30
L32 26 S L27 NOT L28
L33 2 S L32 AND 1/NR

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L34          24 S L32 NOT L33
L35          13 S L34 AND NR>=1
L36          11 S L34 NOT L35
L37           8 S L36 NOT UNSPECIFIED
L38           7 S L37 AND 3/NC
L39          25 S L31,L38
                SEL RN L14
L40         716 S E11-E29/CRN
L41         217 S L40 NOT (MXS OR PMS)/CI
L42          81 S L41 NOT COMPD
L43          66 S L42 AND 2/NR
L44          63 S L43 NOT CONJUGATE

     FILE 'HCAPLUS' ENTERED AT 07:05:54 ON 14 MAR 2006

     FILE 'REGISTRY' ENTERED AT 07:06:11 ON 14 MAR 2006
L45          82 S L14,L44

     FILE 'HCAPLUS' ENTERED AT 07:06:32 ON 14 MAR 2006
L46        2461 S L45
L47        3399 S HYDROXY(1W)NAPHTHOIC ACID
L48          36 S CARBOXY(1W)NAPHTHOL
L49        2584 S HYDROXYNAPHTHOIC ACID
L50         269 S HYDROXY(1W)NAPHTHALENECARBOXYLIC ACID
L51          11 S HYDROXY(1W)NAPHTHALENE CARBOXYLIC ACID
L52         656 S HYDROXY(1W)NAPHTHOATE
L53         332 S HYDROXYNAPHTHALENE(1W)CARBOXYLIC ACID
L54        6953 S L45-L53
L55        6097 S L39
L56        8320 S (LACTIDE OR LACTIC OR POLYLACTI?)(S)(GLYCOLIDE OR GLYCOLIC OR
L57         108 S RESOMER()(RG502H OR RG858 OR RG 858 OR RG 502H OR RG 502 H)
L58          69 S POLYGLACTIN 910
L59         600 S POLYLACTIDE ?GLYCOLIDE
L60         138 S POLYGLACTIN
L61         161 S ATRIGEL OR VICRYL
L62          73 S RESOMER()(RG502 OR RG 502)
L63         468 S RESOMER
L64        8924 S L55-L63
L65           9 S L54 AND L64
L66           5 S L65 AND (PHARMACEUT? OR PHARMACOL?)/SC,SX
L67          50 S L46(L)(THU OR DMA OR PKT OR PAC OR BAC OR FFD OR COS OR DGN)/
L68        4559 S L55(L)(THU OR DMA OR PKT OR PAC OR BAC OR FFD OR COS OR DGN)/
L69           5 S L67,L68 AND L65
L70           5 S L66,L69
L71           4 S L65 NOT L70
L72           3 S L1-L7 AND L65
L73           5 S L70,L72
                SEL HIT RN L73

     FILE 'REGISTRY' ENTERED AT 07:17:47 ON 14 MAR 2006
L74           7 S E30-E36
L75           5 S L74 AND L45
L76           2 S L74 AND L39

     FILE 'REGISTRY' ENTERED AT 07:18:19 ON 14 MAR 2006

     FILE 'HCAPLUS' ENTERED AT 07:18:39 ON 14 MAR 2006

     FILE 'WPIX' ENTERED AT 07:19:19 ON 14 MAR 2006
L77        1232 S L47-L53
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L78           1 S L1
L79           1 S R06285/SDCN OR R00009/SDCN
L80           1 S (R00448 OR R09538)/SDCN
L81           1 S R09404/SDCN
L82           1 S  R09405/SDCN
                E C11H8O3/MF
                E C11 H8 O3/MF
L83          22 S E3
                SEL SDCN 6 14 15 18 22
                EDIT /SDCN /DCN
L84         116 S E1-E5
                SEL DCSE L83 6 14 15 18 22
                EDIT E6-E10 /DCSE /DCRE
L85          96 S E6-E10
L86        1304 S L77,L84,L85 OR L83/DCR
                E LACTIC ACID/CN
L87          18 S E3-E17,E20,E21,E23
L88          18 S L79,L87
                SEL SDCN
                EDIT /SDCN /DCN
L89        5350 S E1-E20
                SEL DCSE L88
                EDIT E21-E38 /DCSE /DCRE
L90        3122 S E21-E38
L91        5355 S L89,L90
                E GLYCOLIC ACID/CN
L92           5 S E3-E6,E9
                SEL SDCN
                EDIT /SDCN /DCN
L93        2240 S E1-E6
L94        2577 S 0448/DRN
                SEL DCSE L92
                EDIT E7-E11 /DCSE /DCRE
L95        1304 S E7-E11
L96        2902 S L93-L95
L97           3 S L86 AND L91 AND L96
                E POLYLACT/CN
L98           2 S E4,E5
                E POLYGLYCOL/CN
L99           2 S E4-E6
L100          4 S L98,L99
                SEL SDCN
                EDIT /SDCN /DCN
L101       6132 S E1-E6
L102       7708 S 0009/DRN
                SEL DCSE L100
                EDIT /DCSE /DCRE E7-E10 /DCSE /DCRE
L103       3975 S E7-E10
L104         10 S L86 AND L101-L103
L105         10 S L104,L97
L106         10 S L105 AND A61K/IPC
L107          3 S L106 AND A61K009-52/IC,ICM,ICS,ICA,ICI
L108          0 S L106 AND A61K009:52/ICI
L109          3 S L106 AND (R051 OR R052)/MO,M1,M2,M3,M4,M5,M6
L110          5 S L106 AND (B12-M10? OR C12-M10?)/MC
L111          4 S L106 AND TAKEDA?/PA
L112          3 S L106 AND (IGARI ? OR HATA ? OR YAMAMOTO ? OR YASUTAKA ? OR YO
L113          6 S L107,L109-L112
L114          4 S L106 NOT L113
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FILE 'WPIX' ENTERED AT 07:36:46 ON 14 MAR 2006

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